

**CHARACTERIZING FALL PREVENTION STRATEGIES, FEAR OF FALLING,  
AND PHYSICAL ACTIVITY AMONG VISUALLY IMPAIRED OLDER ADULTS**

by  
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A dissertation submitted to Johns Hopkins University in conformity with the requirements for  
the degree of Doctor of Science

Baltimore, Maryland

July 2020

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## **Abstract**

Falls are the leading cause of morbidity and mortality among older adults worldwide. At least 30% of community-dwelling adults aged 65 years or older fall at least once each year worldwide. Fall survivors suffer various consequences, including hip fractures, physical activity limitations, and less social engagement, each of which affects overall well-being and quality of life. Older adults with reduced vision have 2- to 8-fold higher risk of falls and injurious falls compared to older adults without visual impairment. Given the lack of therapies to restore vision, the high prevalence of older people with vision loss, and increased risk of falls with age, fall prevention among visually impaired older adults is a critical public health issue.

Previous randomized controlled trials and systematic reviews have examined various fall prevention strategies and programs. However, the majority of previous studies have not accounted for physical activity levels in the analyses. Assessing the effectiveness of fall prevention without accounting for physical activity levels has major limitations because those with fear of falling (FoF) may reduce daily physical activity to avoid falling. Therefore, fall prevention programs not accounting for physical activity limitation may be missing a critical element and opportunity for intervention. Moreover, little research has studied the impact of FoF on activity restriction as an essential component of health and quality of life among older adults with poor vision. A comprehensive understanding of the contribution of physical activity, as well as environmental and behavioral factors, to fall risk will provide opportunities for future interventions to prevent falls and enhance quality of life for older adults with visual impairment.

Visual impairment from several conditions has been associated with lower physical activity; however, the impact of visual damage on patterns of daily physical activity is less studied. Detailing the way in which daily activity is accumulated via objectively measured physical activity may provide critical insights into the characteristics and trajectories of physical activity patterns strongly associated with vision. Novel measures of activity patterns, such as activity fragmentation and diurnal patterns of activity, may provide insights into health and functional status for visually impaired older adults and provide targets for interventions.

The work presented in this dissertation: (1) updated a Cochrane systematic review on environmental and behavioral interventions for preventing falls and reducing physical activity declines in visually impaired older adults, (2) characterized the impact of FoF on physical activity and future falls, and (3) defined and quantified patterns of objectively measured daily physical activity by level of visual field damage.

## Acknowledgement

*“Create a vision for the life you really want and then work relentlessly  
towards making it a reality”*

*- Roy T. Bennett*

I am highly indebted to my thesis committee members and readers, whose support and contributions have significantly improved this dissertation. To my primary advisor, Dr. Jennifer Schrack, I feel so fortunate to have been able to learn everything from you and appreciate your constant support to me during my time in Hopkins. Thank you for including me into your ENGAGE research group (<https://engageresearchlab.org/>), fostering such an enjoyable learning environment for students, and kind membership. To my co-advisor, Dr. Tianjing Li, thank you for your constant engagement and every academic opportunity at Hopkins that you have made possible for me. I am grateful to work with Cochrane Eye and Vision US US Project (<https://medschool.cuanschutz.edu/ophthalmology/research/cochrane-eyes-and-vision-us-satellite>), your timely and thoughtful feedbacks have greatly improved my understanding of all facets of the research process. Dr. Pradeep Ramulu, the opportunity to continue working with you is the reason that I started this research project. Thank you for meeting with me every week over the past two years, even during the holiday seasons. It has been my privilege to keep working with you. Your clear and sharp mind always inspires me in pursuing research in the field of ophthalmic epidemiology. Dr. George Rebok, thank you for your participation in my schoolwide oral exam and defense. Dr. Stephan Ehrhardt, I am very grateful to be part of the Clinical Trial & Evidence Synthesis track. I have learned tremendously from seminars, journal

clubs and research in progress meetings. Dr. Lisa Reider, thank you for your time reviewing my dissertation.

This research project could not have been completed without the dedication and support from faculty and other researchers in the field. Many heartfelt thanks to Roberta Scherer, Xiangrong Kong, Alden Gross, Adam Spira, Janet Holbrook, Douglas Jabs, Dave Shade, Kay Dickersin, Barbara Hawkins, Mark Van Natta, and Sheriza Baksh. I would also like to acknowledge my coauthors for the Falls in Glaucoma Study (FIGS): Aleksandra Mihailovic, Amal Wanigatunga, Pei-Lun Kuo, Sheila West, David Friedman, and Laura Gitlin.

I am especially grateful for faculty, staff, and fellow students from the Department of Epidemiology: David Celentano, Elizabeth Platz, Fran Burman, Laura Camarata, Jonathan Eichberger, Ayesha Khan, Matt Miller, Riaz Qureshi, Jimmy Le, Lin Wang, Jiajun Wen, Yuanxi Jia, Genie Han, Kolade Fapohunda, Olive Tang, Sally Coburn, Lucy Qiao, Batel Blechter, Maneet Kaur, Zhi Yu, Daniel Penaloza, Dylan Duchan, Brooke Jarrett, Forrest Jones, Jowanna Malone, Pablo Martinez Amezcua, Danielle Powell, Chinenye Ugoji, Yurun Cai and Fangyu Liu.

I dedicate this dissertation to my parents who have supported my study in the United States for eight years. To my wife Liby Wang, an MPH student in the Department of Health Policy and Management at Hopkins. Thank you for your constant love, encouragement, and your sacrifices to help me through this journey. To my lovely sons, Charly and William, I enjoy every day to have you in my life.

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# Chapter 1

## **Burden of falls in older adults with visual impairment**

Falls have substantial impact at both the individual and societal levels. These negative impacts are more severe among older adults with visual impairment, who are more likely to experience injurious falls than those without vision impairment.<sup>1</sup> Black and colleagues found that 44% of older visually impaired adults had at least one fall and 31% experienced an injurious fall over one year of study.<sup>2</sup> Haymes and colleagues noted a 2- to 8-fold higher risk of falls and injurious falls in visually impaired older people compared to those with in normal vision (est. annual rate of falls is 10% for older adults with normal vision).<sup>3</sup> Previous studies have estimated the cost of each injurious fall to be between \$3,500 and \$10,700.<sup>4</sup> Since over 3 million Americans suffer from visual impairment, the annual costs of falls in older visually impaired Americans is likely to exceed \$10 billion.

Fall prevention among older adults is critical given the lack of therapies to restore irreversible vision loss. Not only do falls lead to substantial burdens to individuals, healthcare providers, and the health care system,<sup>5</sup> but fall survivors may become less socially engaged and experience increasing risk of depression, both of which are important for overall quality of life.<sup>6,7</sup> More importantly, the impact of falls on the individual can be long-lasting due to the consequence of fear of falling (FoF). Individuals living with a greater FoF are more likely to transition to dependence in activities of daily living, rarely traveling outside of home, and are more likely to be depressed.<sup>8</sup> The development of interventions to prevent falls in high-risk older adults with visual impairment offers a unique opportunity to improve overall health outcomes in this population.

### **Evidence for fall prevention in visually impaired older adults**

A 2018 review by the US Preventive Service Task Force (USPSTF) evaluated interventions to prevent falls in community-dwelling older adults.<sup>9</sup> The USPSTF recommends, with moderate certainty, that exercise programs can prevent falls among community-dwelling adults 65 years or older.<sup>9</sup> However, this review did not focus on visually impaired older adults who are at much higher risk of falls.

Current strategies to prevent falls in visually impaired older adults are to improve confidence and skills in daily life or to change the environmental build at home, work, or leisure to be more accommodative to visual impairment. A Cochrane systematic review published in 2013 searched for evidence from randomized control trials (RCTs) to assess the effectiveness of environmental and behavioral interventions to prevent falls and improve quality of life in older adults with irreversible vision impairment, who lived in the community or residential settings.<sup>10</sup> At the time of the review, Skelton and colleagues found no completed trials meeting the inclusion criteria, although they identified a few ongoing trials.

### **Urgent need to update the 2013 Cochrane review**

Since then, a number of trials have been published. In 2015, Gleeson and colleagues reported that the Alexander technique, designed to alter and improve the way individuals move and react to physical stimuli, was not useful to prevent falls and reduce fear of falling over 12 months for visually impaired older adults in Australia.<sup>11</sup> More recently in 2016, Waterman and colleagues conducted a community-based feasibility trial in England comprising home safety and home

exercise programs implemented by occupational therapists to prevent falls in older people with sight impairment. Although it was acceptable and feasible to deliver home safety and home exercise fall prevention strategies in the community, the study did not find differences between the groups in falls over 6 months.<sup>12</sup> A more recent review by Gillespie and colleagues showed that home hazard modifications were effective in reducing falls in a subgroup of older adults with high risk of falling.<sup>13</sup> Gillespie and colleagues found home safety assessment led by occupational therapists was more effective at reducing the rate of falls compared to home safety assessment led by non-occupational therapists. Additionally, several more trials were published recently in the US, New Zealand and Hungary investigated the efficacy of a variety of environmental and behavioral interventions on preventing falls, reducing physical activity limitation, and improving quality of life in older adults with low vision. The 2013 Cochrane review needs to be updated to include the latest evidence.

### **The main pitfall: fall prevention strategies often neglect physical activity restriction**

One common way to prevent falls is to restrict physical activity, thus reducing the risk of falling by reducing time spent active. Mobility complaints are present in about half of visually impaired patients. Concerns about outdoor mobility tasks such as navigating curbs, shopping, and walking on the streets are the most common complaints from patients with visual impairment<sup>14</sup> Additionally, mobility is highly valued among all older adults and necessary for independent living.

### **Assessing the effectiveness of fall prevention without addressing mobility restrictions has major limitations**

Individuals with greater Fear of Falling (FoF) could reduce the incidence of falls by restricting mobility in the short term,<sup>15</sup> but this copying strategy adversely affects overall well-being in the long term. Falls and the resultant FoF, are plausible intermediaries bridging poor visual function with decreased mobility.<sup>16</sup> Preliminary data from the Falls in Glaucoma Study (FIGS) have shown that greater FoF levels were strongly associated with decreased physical activity: a cross-sectional study reported a reduction of 2,000 daily steps from mild/none to moderate FoF and a further reduction of 2,000 daily steps from moderate to severe FoF. Furthermore, vision loss was no longer associated with lower physical activity or decreased travel outside the home when FoF was included in analytic models amongst participants with some forms of vision loss (e.g., age-related macular degeneration).<sup>17</sup> These findings suggest that FoF is likely to be the primary link between loss of visual function and restriction of physical activity and travel outside the home.

### **FoF may serve as an indicator for future falls and physical activity**

There are intrinsic relationships between FoF, physical activity, and future falls risk. People have used the three measurements both as exposures and outcomes, or even as intermediates<sup>18,19</sup>. Previously, the links between FoF and future fall risk, and real-world mobility outcomes (i.e., physical activity and travel outside the home) have been assessed cross-sectionally in visually impaired patients.<sup>20,21</sup> The relationships among these measurements in longitudinal settings are yet to be explored. Longitudinal studies yielding multiple or repeated measures on each person can characterize and quantify the individual patterns of change in these associations. While there have been longitudinal studies on physical activity and falls elsewhere, they did not measure activity objectively or collect falls data prospectively.<sup>20,21</sup> Compared to cross-sectional studies, longitudinal analyses can inform how different levels of FoF affect consequent changes in future



risk of falling and restriction of physical activity, while considering the change in FoF over time. If we find FoF to be associated with future falls and physical activity, reducing FoF may help prevent broader future morbidity related to important domains such as falls and physical activity.

### **Characterizing physical activity patterns among visually impaired older adults is highly important**

Visual impairment from several conditions has been associated with lower physical activity,<sup>22-25</sup> with studies specifically demonstrating associations between vision damage and lower amounts of objectively measured daily activity, and less time spent in moderate and vigorous physical activity (MVPA).<sup>22,26,27</sup> Although previous research has found vision damage impacts time spent in MVPA to a similar degree as other systemic conditions (such as arthritis, diabetes, and stroke),<sup>27</sup> the impact of visual damage on patterns of daily physical activity is less studied. For example, daily physical activity becomes less frequent and intense, shorter in length, and more fragmented with age,<sup>28</sup> marking individuals with low physical capacity and endurance,<sup>28,29</sup> and higher future mortality.<sup>30-32</sup> Detailing the manner in which daily activity is accumulated via objectively measured physical activity may provide critical insights into the characteristics and trajectories of physical activity patterns in visually impaired people. These novel measures of activity patterns, such as activity fragmentation and diurnal patterns of activity, may provide insights into health and functional status for visually impaired older adults. Moreover, understanding the patterns of physical activity among visually impaired people may contribute to developing successful fall prevention strategies designed to reduce falls without restricting physical activity.

## **Background summary**

Considering the pervasive nature of suboptimal health in older adults with visual impairment, health promotion strategies to maintain physically active and achieve fall reduction have been recommended specifically for people with vision loss.<sup>33</sup> In addition, the advocates for poor vision community are encouraged to develop innovative and applicable interventions to mitigate environmental and physical barriers faced by persons with visual impairment, so as to lessen the influence of these modifiable factors on overall health of such growing yet undertreated population. To respond to these recommendations, the series of manuscripts within this dissertation lay the groundwork for characterizing fall prevention strategies, increasing physical activity levels and health status of persons with vision-related functional decline.

The overarching goal of this dissertation was to establish an outlet through which visually impaired older adults could become self-promoters of health by leading a physically active and safe lifestyle. The ideal fall prevention strategy is to achieve reduction in falls, enhance safe mobility, and improve confidence in daily living tasks. By systematically reviewing the current literature, this dissertation will improve our understanding about the current strategies to prevent falls and reduce physical activity limitations among visually impaired older adults, how fall outcomes and physical activity are measured in clinical trials, and whether FoF is reported as a primary outcome. Moreover, by using the vast resource of the FIGS, a single-center prospective study, this dissertation aims to characterize the impact of FoF on future falls and measures of physical activity among visually impaired older adults. Finally, uncovering the complex patterns of physical activity in older adults with visual impairment who are largely affected by physical

inactivity and sedentary behaviors, will provide an indicator of future health and risk of functional decline, and highlight opportunities for future interventions.

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## Chapter 2

### Environmental and Behavioral Interventions for Reducing Physical Activity Limitation and Preventing Falls in Older People with Visual Impairment

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Keywords: behavioral; environment; falls; fear of falling; older adults; physical activity; vision loss

Manuscript word count: 14,044

## **Abstract**

**Background:** Impairment of vision is associated with a decrease in activities of daily living. Avoidance of physical activity in older adults with visual impairment can lead to functional decline and is an important risk factor for falls. The rate of falls and fractures is higher in older people with visual impairment than age-matched visually normal older people. Possible interventions to reduce activity restriction and prevent falls include environmental and behavioral interventions.

**Objectives:** We aimed to assess the effectiveness and safety of environmental and behavioral interventions in reducing physical activity limitation, preventing falls and improving quality of life amongst visually impaired older people.

**Search methods:** We searched CENTRAL (which contains the Cochrane Eyes and Vision Trials Register) (Issue 1, 2020), Ovid MEDLINE, EMBASE, CINAHL, Allied and Complementary Medicine Database, OT Seeker, *metaRegister* of Controlled Trials, non-indexed citations, ClinicalTrials.gov and WHO ICTPR to 31 January 2020 with no language restrictions.

**Selection criteria:** Randomized controlled trials (RCTs) and quasi-randomized controlled trials (Q-RCTs) that compared environmental interventions, behavioral interventions or both, versus control (usual care or no intervention), and trials comparing different types of environmental or behavioral interventions, in older people (aged 60 and over) with irreversible visual impairment living in their own home or in residential settings. To be eligible for inclusion, the studies must include a measure of physical activity or falls, the two primary outcomes of interest. Secondary outcomes included fear of falling and quality of life.

Data collection and analysis: We used standard Cochrane methods.

Main results: We included six RCTs (686 participants) conducted in five countries (UK, US, Australia, New Zealand, Hungary) with follow-up periods ranging from 2 to 12 months. These trials included older adults (mean age=80 years) with visual impairments of varying severity and underlying causes, predominately women (69%). Participants mostly lived in their homes and were physically independent. We classified all trials as having high risk of bias for masking of participants, and three trials as having high or unclear risk of bias for all other domains. The included trials evaluated various intervention strategies (e.g., exercise program versus home safety modifications). However, the study characteristics differing across trials, including interventions and outcomes (e.g., different fall measures), precluded any meta-analysis.

Two trials compared the home safety modification by occupational therapists versus social/home visits. One trial (28 participants) reported physical activity at 6 months and showed no difference in mean estimates between groups (step counts: mean difference [MD]=321, 95% confidence interval [CI]: -1981, 2622; average walking time [minutes]: MD=1.70, 95% CI: -24.03, 27.43; telephone questionnaire for self-reported physical activity: MD=-3.68 scores, 95% CI: -20.6, 13.24; low certainty of evidence). Two trials reported the proportion of participants who fell at 6 months (Risk Ratio [RR]=0.76, 95% CI: 0.38, 1.51, 28 participants) and 12 months (RR=0.59, 95% CI: 0.43, 0.80, 196 participants) with low certainty of evidence. One trial (28 participants) reported fear of falling at 6 months using the Short Falls Efficacy Scale-International, and found no difference in mean estimates between groups (MD=2.55 scores, 95% CI: -0.51, 5.61; low certainty of evidence). This trial also reported quality of life at 6 month using 12-Item Short

Form Health Survey, and showed no difference in mean estimates between groups (MD=-3.14 scores, 95% CI: -10.86, 4.58; low certainty of evidence).

Five trials compared behavioral intervention (exercise) versus usual activity or social/home visits. One trial (59 participants) assessed self-reported physical activity at 6 months and showed no difference between groups (MD=9.1 scores, 95% CI=-13.85, 32.5; low certainty of evidence). Three trials investigated different fall measures at 6 or 12 months, and did not find differences in effect estimates (RRs for proportion of fallers ranged from 0.54 [95% CI = 0.29, 1.01, 41 participants] to 0.93 [95% CI: 0.61, 1.39, 120 participants]; with low certainty of evidence). Three trials assessed the fear of falling using Short Falls Efficacy Scale-International or the Illinois Fear of Falling from 2 to 12 months, and found no differences in mean estimates between groups (the estimates ranged from -0.88 score [95% CI: -2.72, 0.96, 114 participants] to 1.00 score [95% CI: -0.13, 2.13, 59 participants]; low certainty of evidence). One trial (59 participants) assessed the European Quality of Life scale at 6 months (MD=-0.15 score, 95% CI: -0.29, -0.01), which was not clinically different between groups (with low certainty of evidence).

Authors' conclusions: There is no evidence of effect for most of the environmental or behavioral interventions studied for reducing physical activity limitation and preventing falls in visually impaired older people. The certainty of evidence is generally low due to poor methodological quality and heterogeneous outcome measurements.

A consensus is needed to adopt standard ways to measure physical activity and falls reliably in older people with visual impairments. Fall prevention trials should plan to use objectively measured or self-reported physical activity as outcome measures, to reduce activity limitation. Future research is needed to evaluate the acceptability and applicability of interventions, and use

validated questionnaires to assess the adherence to rehabilitative strategies and performance during activities of daily living.

## **Plain language summary**

### *1. What is the aim of the review?*

This Cochrane Review aimed to determine if environmental and behavioral interventions can reduce activity limitation and prevent falls in older adults with visual impairment, which included, but not limited to, low visual acuity, poor contrast sensitivity, and reduced visual field. The authors collected and analysed all relevant studies to answer this question and found six studies.

### *2. Key messages*

There is little evidence from randomized controlled trials that suggests environmental or behavioral intervention is more effective than usual care (e.g., social/home visit and usual activity) in reducing activity limitation and preventing falls for older people with visual impairment.

### *3. What was studied in the review?*

Visual impairment in older people is associated with avoidance of physical activity, (e.g., fewer daily steps), anxiety and depression as well as an increased risk of physical disability (e.g., fractures). Behavioral strategies such as exercise programs may improve a person's skill and confidence in physical activity. Environmental changes in the home, work or leisure environment, such as improved lighting or highlighting stair edges both outside and inside the home, may help reduce activity restriction, prevent falls and improve quality of life. We searched for evidence from trials of environmental or behavioral interventions in older adults living in

their own home or residential settings, with irreversible vision impairment (e.g., due to aging, diabetes, or drugs side effects), which aimed to reduce activity restriction and prevent falls.

#### *4. What are the main results of the review?*

We included six trials with a total of 686 older people with visual impairment and a variety of other reported disabilities, who lived independently or in residential settings. No evidence of effect was shown for most of the environmental or behavioral interventions studied for reducing physical activity limitation and preventing falls in visually impaired older people. We found low certainty of evidence that the environmental interventions, particularly home safety modification delivered by occupational therapists, may have a small benefit on preventing falls compared with social/home visits. However, such environmental interventions did not appear to have an impact on physical activity. No evidence of benefit was observed in other types of behavioral interventions that aimed to reduce activity limitation and prevent falls, but the certainty of evidence is low.

#### *5. How up-to-date is this review?*

Cochrane Review authors searched for studies published up to 31 January 2020



## Background

The prevalence of visual impairment is estimated by the World Health Organization (WHO) to be 285 million worldwide.<sup>1</sup> One in eight people in the UK over the age of 75 and one in three over the age of 90 live with significant sight loss.<sup>2</sup> Older adults with visual impairment are more likely to be physically dependent,<sup>3</sup> have higher risk of moving into residential settings (e.g., nursing homes and long-term care settings),<sup>4,5</sup> and have poorer functions in daily livings<sup>6,7</sup> than normally sighted peers. Vision deterioration is also associated with adverse health consequences among older people, especially with regard to activity limitations.<sup>8</sup> These include decreases in leisure activities, Instrumental Activities of Daily Living performance and social function, Activities of Daily Living and compromised mobility. The International Classification of Functioning defines activity as "the nature and extent of performance of a function by a person" and activity limitations as "problems of the performance of activities in nature, duration, and quality".<sup>9</sup> Avoidance or lack of physical activity by older adults with low vision may have implications for other health problems, such that social isolation, anxiety and depression should be noted by ophthalmologists and others treating these populations.<sup>10</sup> Challenging environments, struggling to obtain transportation, feelings of vulnerability, having decreased energy, and lacking assertiveness were all identified in interviews with older visually impaired adults as reasons for not being physically active and not feeling competent in such activities.<sup>10</sup>

Visual impairment is associated with an increase in the incidence of falls, hip fractures, and depression.<sup>11</sup> Avoidance of physical activity because of fear of falling is common among older people at risk of falling.<sup>12</sup> Indeed, the rate of falls in older people with visual impairment is 1.7 times higher, and hip fractures are 1.3 to 1.9 times higher than in age-matched visually normal

populations.<sup>13</sup> One study reported that activity restriction was present in 45% of those with visual impairment, compared with only 24% in those without visual impairment who had experienced an injurious fall.<sup>14</sup> Those with visual impairment were also more likely to admit to fear of falling (44%) even without a fall history. One study has shown that perceived interference of vision loss on goal-directed behavior and expected activities has greater influence on distress and is subsequently predictive of disability in comparison with objective symptoms (visual acuity).<sup>15</sup> It therefore seems likely that the mechanism underpinning previous trials of maintaining physical activity and preventing falls, particularly with respect to environmental components, behavioral components or both, for people with visual impairment will be different from the general population.

### **Description of the condition**

Visual impairment is defined as best-corrected visual acuity of the better eye less than 0.3 logMAR (Log of the Minimum Angle of Resolution) units or visual field defects within 20 degrees of fixation. Blindness is defined as visual acuity less than 0.05 logMAR units or visual field defects within 10 degrees of fixation.<sup>16</sup> A working definition of visual impairment is low vision that cannot be corrected by standard glasses or by medical or surgical intervention. The top five conditions leading to visual impairment in the US are diabetic retinopathy, age-related macular degeneration, cataract, glaucoma, and eye injury or trauma.<sup>17</sup> Age-related macular degeneration and diabetic retinopathy are the most common causes of blindness in Americans over 65 years of age.<sup>18</sup>

### **Description of the intervention**

Environmental interventions include any targeted, intentional improvement to the usually indoor physical environment, with the aim of reducing symptoms or improving well-being.<sup>18</sup> In the case of visual impairment, this may incorporate adaptations and modifications to an individual's physical environment (usually their home) as the result of a formal environmental assessment that identified potential hazards or restrictions. The aim of the environmental intervention is to enhance the individual's ability to perform daily living tasks safely and independently, facilitating their safe mobility and improving confidence. Examples of environmental interventions for individuals with visual impairment include the removal of rugs, increased lighting in hallways and applying contrasting stripes on stairs.

Behavioral interventions include the systematic implementation of procedures that result in lasting positive changes in an individual's behaviour.<sup>19</sup> These interventions, for people with visual impairment, might include, but are not restricted to, the teaching of adaptive strategies to enhance changes in an individual's behavior when navigating and interacting with their environment<sup>20</sup> and orientation and mobility training.<sup>21</sup> Orientation and mobility training aims to teach visually impaired people how to ambulate and navigate the environment safely and independently and may contribute to reduced activity limitations and societal participation.<sup>22</sup>

Occupational therapists, as a profession, have the expertise to assess, devise and implement rehabilitation plans which incorporate both types of interventions: an occupational therapy approach encompasses both environmental change and the interaction of the individual with their environment, their actions and their behavioral adaptations at home and in the community. This dynamic relationship between the person, their behavior and the environment has been described elsewhere.<sup>20,23</sup> Many environmental risk assessments, and some environmental modifications, are

undertaken by other professionals but the relationship of the person, their behavior and their environment may not be evaluated comprehensively.

### **How the intervention might work**

Through changes in the home environment and behavioral strategies, the person with visual impairment may feel more confident that they can navigate their environment safely, thereby reducing concerns about their safety and fear of falling. This improved muscle strength and balance may lead to greater mobility and habitual physical activity, and lower risk of falling. Although increased physical activity can increase exposure to falls, studies with exercise interventions which focus on stability and strength have been shown not to increase risk of falls.<sup>8,24,25</sup>

### **Why it is important to do this review**

Avoidance of activity is more common and the risk of falls is greater in older people with visual impairment than those with normal vision. Although there exists a suite of Cochrane reviews on falls prevention in older people living in the community,<sup>26,27</sup> in residential settings<sup>28</sup> and on exercise to reduce fear of falling,<sup>29</sup> they do not include all studies in participants with specific conditions (those with visual impairment) or do not have any sub-analyses on those studies in older people with visual impairment.

The physiological, psychological, functional and societal benefits of regular physical activity amongst older people are irrefutable.<sup>30</sup> Interventions that improve habitual physical activity in visually impaired older people are vital to promoting public health. Trials which have adopted a holistic, participant-centered approach (such as environment modification led by occupational

therapies) have shown reductions in falls both within and outside the home), whereas trials that have considered removal of home hazards only did not reduce the incidence of falls, even within the home. One potential mechanism for falls reduction could be that the visually impaired individual actually restricts activity more as a result of the intervention, which in the short term could reduce exposure to falls risk. There is therefore a need to further unpick the mechanism of reduction in falls as well as maintaining or increasing physical activity in visually impaired older people. Since trials have rarely considered activity restriction alongside falls as an outcome measure, the effectiveness and safety of environmental and behavioral interventions remain unclear.

Seven years have passed since the original version of this review was published,<sup>31</sup> which found no eligible studies, the topic of maintaining physical activity and preventing falls in older adults with vision impairment remains highly relevant to patients, care givers, providers, insurers, and policy makers. Therefore, an update is needed to examine the recent evidence with regard to the effect of environmental or behavioral interventions for reducing physical activity limitation and preventing falls in visually impaired older people.

## **Objectives**

The objective of this review was to assess the effectiveness and safety of environmental and behavioral interventions in reducing activity limitation, preventing falls, and improving quality of life amongst visually impaired older people.

## **Methods**

## *Criteria for considering studies for this review*

### 1. Types of studies

We included randomized controlled trials (RCTs) and quasi-randomized controlled trials (Q-RCTs) that compared environmental interventions, behavioral interventions or both, versus control (placebo control or no intervention or usual care), and trials comparing different types of environmental or behavioral interventions. We did not include studies that report only quality of life (as opposed to limitations in mobility and quality of life) so as to avoid overlap with another Cochrane review.<sup>32</sup>

### 2. Types of participants

We included trials with the following participants:

- Older people (aged 60 and over) with irreversible visual impairment including, but not limited to, low visual acuity, poor contrast sensitivity, poor depth perception and reduced visual field.
- Older people with irreversible visual impairment and other multiple disabilities, such as hearing loss, neurological or musculoskeletal disease or cognitive impairments.
- Older people living independently and those living in residential settings.

### 3. Types of interventions

Environmental interventions, behavioral interventions or both, including but not limited to visual rehabilitation (e.g. low vision devices), removal of home hazards, home safety modifications,

provision of adaptive or assistive equipment, advice on behavioral changes to improve safety in activities of daily living, cognitive behavioral therapies, or other behavioral therapies.

For any study included, we aimed to record the professional training of the person delivering the interventions. The types of interventions would also be rated on the intensity of the intervention, based on previously published criteria (evaluation of risk of person and environment; validated assessment tools; formal or observational evaluation of functional capacity; and adequate follow-up).<sup>33</sup>

We did not include other vision-correction interventions (e.g. cataract surgery, corrective lenses or filters) in this review.

#### 4. Types of outcome measures

Primary outcomes:

To be eligible for inclusion, the studies need to measure physical activity or falls. The primary outcomes were analyzed at 12 months of follow-up.

A measure of physical activity:

- Continuous objective measures, e.g., body fixed sensor activity monitoring.
- Continuous self-reported measures, e.g., validated questionnaires such as Physical Activity Scale for the Elderly, Community Healthy Activities Model Program for Seniors.
- Other self-reported measures, which may be dichotomous, e.g., single questions on physical activity.

A measure of falls:

- Falls (number of fallers or rate of falls) and injurious falls. Prospective daily calendars returned monthly for at least one year is the preferred method for recording falls.<sup>34</sup>

Secondary outcomes:

Our secondary outcomes, also analyzed at 12 months of follow-up, included the following:

- Fear of Falling, e.g., Short Falls Efficacy Scale-International (SFES-I) and the University of Illinois at Chicago Fear of Falling Measure.
- Quality of life, e.g., European Quality of Life (EuroQoL), 12-Item Short Form Health Survey (SF-12), 36-Item Short Form Health Survey.
- Attitudes, beliefs and behaviors, e.g., Attitudes to Falls-Related Interventions Scale, Fear-Avoidance Beliefs Questionnaire. The latter may also be ascertained via qualitative methods such as focus groups and interviews.

Follow-up:

As the frequency and duration of environmental and behavioral interventions varied depending on feasibility and severity of visual impairment, we used the time points (longer than or equal to 2 months) for outcome assessment as reported in each included trial in addition to 12 months.

## **Search methods for identification of studies**

### *1. Electronic searches*



We searched the Cochrane Central Register of Controlled Trials (CENTRAL) 2020, Issue 1, part of The Cochrane Library. [www.thecochranelibrary.com](http://www.thecochranelibrary.com) (accessed 31 January 2020), Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid MEDLINE Daily, Ovid OLDMEDLINE, (January 1950 to January 2020), EMBASE (January 1980 to January 2020), Cumulative Index to Nursing and Allied Health Literature (CINAHL) (January 1937 to January 2020), Allied and Complementary Medicine Database (AMED) (January 1985 to January 2020), the metaRegister of Controlled Trials (mRCT) ([www.controlled-trials.com](http://www.controlled-trials.com)), ClinicalTrials.gov ([www.clinicaltrials.gov](http://www.clinicaltrials.gov)) and the WHO International Clinical Trials Registry Platform (ICTRP) ([www.who.int/ictip/search/en](http://www.who.int/ictip/search/en)). We did not use any date or language restrictions in the electronic searches for trials. We last searched the electronic databases on 31 January 2020.

See: Appendices for details of search strategies for CENTRAL (Appendix 1), MEDLINE (Appendix 2), EMBASE (Appendix 3), CINAHL (Appendix 4), AMED (Appendix 5), OTseeker (Appendix 6), mRCT (Appendix 7), ClinicalTrials.gov (Appendix 8) and the ICTRP (Appendix 9).

## *2. Searching other resources*

We contacted authors of any ongoing trials or abstracts found, and searched the reference lists of full papers reviewed, as identified in our electronic search.

## **Data collection and analysis**

### *1. Selection of studies*

Two review authors, working independently, screened all titles and abstracts. Two review authors assessed the full-text articles of the selected titles and abstracts for eligibility outlined above. We resolved disagreements by consensus. In one instance for an abstract we sought additional information from the author; however, the study did not meet the inclusion criteria.

### *2. Data extraction and management*

When a study fulfilled the inclusion criteria, data concerning methodological issues, characteristics of participants, interventions and outcome measures were independently extracted using a standard Covidence extraction form. The review authors were not masked to the study authors, institutions or journal of publication. Where available and appropriate, we have presented quantitative data for the outcomes listed in the inclusion criteria in the analyses. Where studies reported standard errors of the means (SEs), we obtained standard deviations (SDs) by multiplying SEs by the square-root of the sample size. We attempted to contact authors of studies where there was inadequate reporting of data, to enable clarification and where appropriate.

### *3. Assessment of risk of bias in included studies*

Two review authors worked independently to assess risk of bias in included studies using the methodology described in Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions*.<sup>35</sup> The studies were assessed on the following criteria: random sequence generation, allocation concealment, masking (blinding) of participants and personnel, masking of outcome assessment, incomplete outcome data, selective outcome reporting and other sources of

bias. Due to the nature of interventions, it was not possible to mask participants or staff providing the intervention. It was however possible to mask outcome assessors for measurements. Authors' assessments were 'high risk of bias', 'low risk of bias' or 'unclear risk of bias'.

#### *4. Measures of treatment effect*

For each trial, we calculated a risk ratio (RR) and 95% confidence interval (CI) for dichotomous outcomes, and mean differences (MD) and 95% CI for continuous outcomes (reporting mean and SD). We planned to calculate standardized mean differences (SMDs) and 95% CIs when combining results from studies using different ways of measuring the same concept.

#### *5. Unit of analysis issues*

We reported the level at which randomization occurred in the included studies, as described in Chapter 9 of the *Cochrane Handbook for Systematic Reviews of Interventions*.<sup>35</sup> When individual was randomized, the unit of analysis was at individual level. Possible variations in study designs included cluster-randomized trials and cross-over trials. When such trials were available, we planned to assess whether trials had properly accounted for the intracluster or intraperson correlation.

#### *6. Dealing with missing data*

We analyzed available-case data as reported by assuming missing at random. We did not impute any missing data. We described the potential effect of missing data upon conclusions drawn from this review.

### *7. Assessment of heterogeneity*

We assessed clinical heterogeneity by examining characteristics of individual studies. We assessed methodological heterogeneity by comparing study design and risk of bias across the trials. We planned to test statistical heterogeneity using the value of  $I^2$  when meta-analysis was feasible, i.e., a value greater than 50% might indicate substantial heterogeneity.<sup>36</sup> In the presence of heterogeneity, depending on the number of studies and the direction of effect, we would have combined the results of comparable groups of trials using the random-effects model and would have considered the subgroup analyses described later.

### *8. Assessment of reporting biases*

We would have tested small study effects which could be due to reporting bias using funnel plots when there was a sufficient number of trials (10 or more).

### *9. Data synthesis*

We did not combine study results due to substantial clinical or statistical heterogeneity, but provided the effect estimates and associated CIs for individual trials. Where appropriate, we would have pooled results of comparable groups of studies using the random-effects model and calculated 95% CIs.

### *10. Subgroup analysis and investigation of heterogeneity*

The review authors considered the following hypotheses using subgroup analysis if sufficient data were available:

1. Are interventions equally effective on differing severities of visual impairment?
2. Are interventions equally effective with fallers at baseline as they are with the general older population?

There were insufficient data to look at these questions.

### *11. Sensitivity analysis*

We planned to undertake sensitivity analyses, where indicated, to investigate the effects of methodological quality. For example, if appropriate, we would have looked at the effect of excluding Q-RCTs, as they would be at higher risk of selection bias. As no Q-RCTs were identified for inclusion in this review and there were low number of trials eligible for each comparison, we were unable to undertake such analyses.

### *12. Grading of evidence and summary of findings table*

We presented major outcomes (including physical activity, falls, fear of falling, and quality of life) in the 'Summary of findings' tables. We graded the quality of evidence per outcome (high, moderate, low and very low) for two main comparisons (environmental intervention versus social/home visit, and behavioral intervention versus usual activity or social/home visit) using the GRADE approach,<sup>35</sup> and documented concerns relating to reasons of downgrading accordingly.

## **Results**

## *Description of studies*

### Results of the search

In the original version of this review, the electronic searches yielded a total of 6014 references from electronic databases, screening citations from relevant references. After removing duplicates and irrelevant reports, the authors screened the remaining 780 published reports to identify potentially relevant studies, and obtained full-text copies of 30 studies. After reading the full-text record, the authors excluded these studies, while finding five ongoing studies.

We updated the search on January 31, 2020 and identified 2171 new records (Figure 1). We removed 27 duplicates and screened 2144 titles and abstracts for eligibility, of which 62 were obtained for full-text screening. After removing 1 ongoing study and 55 reports with reasons, we included one trial previously awaiting classification,<sup>37</sup> one trial<sup>38</sup> that only reported fall-related outcomes and was excluded in previous review, and four new trials<sup>39-42</sup>. Altogether, we included six trials for this updated review, as well as one ongoing trial.<sup>43</sup>

## *Included studies*

### 1. Study design

The six included RCTs were described in “Characteristics of included studies.” Four of the included trials randomized participants to one of two treatment groups, either environmental or behavioral intervention versus a control. One trial had three<sup>37</sup> and another trial had four treatment groups<sup>38</sup>, including both environmental and behavioral interventions. The included trials were published between 2005 and 2018.

## 2. Participants

The participants, 686 in total, were recruited from five countries (Australia, Hungary, New Zealand, UK, US). These trials varied in sample size, from 21 participants in the smallest trial<sup>41</sup> to 391 participants in the largest trial<sup>38</sup>. Four trials included participants with varying severity and causes of visual impairment<sup>37-39,42</sup>, one with age-related macular degeneration only<sup>40</sup> and one with blindness<sup>41</sup>. Five trials included participants with an average age of 60 or older<sup>37-40,42</sup>, and one with a median age of 59<sup>41</sup> (we included this trial because half of participants were over 60). Five trials included both men and women<sup>37-40,42</sup> and one included only women<sup>42</sup>. Overall, the follow-up periods ranged from 8 weeks to 12 months. Five out of six trials enrolled participants living independently in the community<sup>37-41</sup> and one trial recruited participants living in nursing homes<sup>42</sup>.

We observed clinical heterogeneity across six trials, including age, sex, reason and severity of visual impairments, and prior experience of environmental and behavioral training. Since older age at study enrolment, female sex, and poorer vision are associated with lower physical activity and higher risk of falls,<sup>44-46</sup> the responses to environmental and behavioral interventions could vary by these factors.

## 3. Interventions

The included trials investigated a broad range of environmental and behavioral interventions. Two trials evaluated environmental interventions compared with social/home visits<sup>37,39</sup>. Specifically, in Campbell 2005<sup>38</sup>, occupational therapists visited the participants at home and assessed home safety using a checklist. They discussed potential hazards in the home that could

lead to falls and implemented home modifications. In Waterman 2016<sup>37</sup>, occupational therapists discussed environmental hazards present in their homes with participants, and jointly agreed upon an action plan about how to alter their environment to reduce risk of falls. The social/home visit was conducted by volunteers to provide social support and discuss general topics about lifestyles without giving any clinical advice. Five trials assessed the behavioral interventions versus usual activities or social/home visits<sup>38-42</sup>. These trials considered various behavioral interventions that were carried out by a greater range of healthcare professionals, including physiotherapists, occupational therapists and other exercise professionals. These behavioral interventions included the multi-component Falls Management Exercise program<sup>39</sup>, the Otago exercise program to improve muscle strength and balance<sup>38</sup>, the Alexander technique to improve movement and reaction to physical stimuli,<sup>40</sup> and Ashtanga-based Yoga therapy to alter stability and balance.<sup>41</sup> Two trials evaluated the combination of home hazard modifications and Otago exercise program compared with social/home visits.<sup>37,38</sup>

#### 4. Outcomes

Two trials evaluated physical activity over 6 months follow-up.<sup>37,39</sup> Both trials reported a telephone questionnaire for self-reported physical activity at 6 months, one trial used an instrumented monitoring of physical activity using a body fixed sensor at 6 months.<sup>37</sup>

Four trials assessed a variety of measures of falls with study duration ranging from 2 to 12 months.<sup>37,38,40,42</sup> Specifically, Kovacs 2012<sup>42</sup> reported number of fallers at 2 months and mean length of time to first fall. Gleeson 2017<sup>40</sup> reported number of fallers and fall rate per person at 12 months. Waterman 2016<sup>37</sup> reported number of fallers and injurious fallers at 6 months. Campbell 2005<sup>38</sup> reported number of fallers and injurious fallers at 12 months, falls per person



year, injurious falls per person year, incidence rate ratio for falls and incidence rate ratio for injurious falls.

Four trials assessed fear of falling using different instruments with study durations ranging from 2 to 6 months.<sup>37,39-41</sup> Specifically, Jeter 2015<sup>41</sup> used the University of Illinois at Chicago Fear of Falling measured at 2 months, and three trials used the SFES-I instrument at 3 months<sup>40</sup> and 6 months.<sup>37,39</sup>

Quality of Life measures, as one of the secondary outcomes, were also reported, including EuroQoL,<sup>39</sup> SF-12,<sup>37</sup> Geriatric Depression Scale,<sup>40</sup> and Positive and Negative Affect Scale.<sup>40</sup> No adverse events due to the interventions were reported.

#### *Excluded studies*

Of 55 excluded studies, 21 (38%) were non-randomized or quasi-randomized controlled trial, 17 (31%) did not measure the outcomes of interest, 12 (22%) did not report the comparison of interest, and 5 (9%) did not study the population of interest

#### *Risk of bias in included studies*

We evaluated the risk of bias for each trial using seven prespecified criteria summarized in (Figure 2).

### *1. Sequence generation*

We assessed six trials at low risk of bias for sequence generation.<sup>37-42</sup> All six trials used computer software to generate the random sequence.

### *2. Allocation concealment*

We judged six trials at low risk of bias for allocation concealment. Five trials reported the coordinators of group assignments did not know the next assignment when implementing the randomization,<sup>37-41</sup> and Kovacs 2012<sup>42</sup> used sealed, opaque envelopes.

### *3. Blinding of participants and personnel (performance bias)*

It was not possible to mask participants or persons involved in the trial due to the nature of interventions. We judged all six trials at a high risk of bias for blinding of participants and personnel.<sup>37-42</sup>

### *4. Blinding of outcome assessment (detection bias)*

Five trials adequately described that outcome assessors remained masked to group allocation, and were judged as a low risk of bias.<sup>37,38,40-42</sup> But Adam 2018<sup>39</sup> did not report whether outcome assessor was masked and was classified as unclear risk of bias for this domain.

### *5. Incomplete outcome data (attrition bias)*

We provided the number of participants who were lost to follow-up or excluded after randomization in each trial (Characteristics of included studies). Five of six trials, we considered as a low risk of bias because intention-to-treat analysis were adequately conducted, number of

dropouts were balanced between arms, or adequate reasons for dropouts were similar between arms.<sup>37-39,41,42</sup> Gleeson 2017<sup>40</sup> reported 10 out of 120 participants did not complete assessments, and was classified as unclear risk of bias for this domain.

#### *6. Selective reporting (reporting bias)*

Four trials reported all prespecified outcomes in the trial registration or protocol, we judged them as at low risk of bias for this domain.<sup>37,38,40,42</sup> Adams 2018<sup>39</sup> failed to show outcomes about activity avoidance and loneliness which were reported in the trial registration, so we assessed it at high risk of bias. Jeter 2015<sup>41</sup> reported results which were a subset of a larger battery of assessments that included psychological questionnaires and other information, we judged the risk of bias to be high.

#### *7. Other potential sources of bias*

We identified no other potential sources of bias in six trials.

### **Effects of interventions**

The study characteristics varied across trials, including interventions and outcomes. As a result, we did not combine the quantitative results in meta-analysis. Instead, we reported the outcomes under each comparison when data were available.

We classified the six trials into six comparisons as described below. One three-arm trial<sup>37</sup> and one four-arm trial<sup>38</sup> contributed to more than one comparison.

- Environmental intervention versus social/home visits: 2 trials (Campbell 2005; Waterman 2016)
- Behavioral intervention versus social/home visits: 5 trials (Adams 2018; Kovacs 2012; Campbell 2005; Gleeson 2017; Jeter 2015<sup>38-42</sup>)
- Environmental intervention versus behavioral: 1 trial (Campbell 2005)<sup>38</sup>
- Environmental and behavioral intervention versus social/home visits: 2 trials (Campbell 2005; Waterman 2016)<sup>37,38</sup>
- Environmental and behavioral intervention versus environmental: 2 trials (Campbell 2005; Waterman 2016)<sup>37,38</sup>
- Environmental and behavioral intervention versus behavioral: 1 trial (Campbell 2005)<sup>38</sup>

See: Summary of findings table 1 and Summary of findings table 2 for the main comparisons.

### *1. Environmental intervention versus social/home visits (2 trials)*

#### Physical activity and falls (2 trials, 224 participants)

Two trials assessed home hazards modification compared with social/home visits (Figure 3) (Campbell 2005; Waterman 2016)<sup>37,38</sup> in older adults with visual impairment and living in the community. The follow-up period ranged from 6 to 12 months.

One trial assessed physical activity at 6 months (Figure 3).<sup>37</sup> Physical activity was measured using step counts, walking time, and self-reported activity (Phone-FITT). There were no significant differences between home hazards modification compared with social/home visits in step counts (MD=321, 95% CI: -1981, 2622, walking time in minutes (MD=1.7, 95% CI: -24.03,

27.43) or self-report activity (MD=-3.68 scores, 95% CI: -20.6, 13.24). The certainty of evidence was low, downgraded for risk of bias (-1) and imprecision (-1).

Two trials investigated a variety measures of falls ranging from 6 to 12 months. Waterman 2016<sup>37</sup> found no significant difference between groups at 6 months using proportion of fallers (RR=0.76, 95% CI: 0.38, 1.51), falls rate per person year (MD=0.74, 95% CI: -0.71, 2.19), moderate injurious falls per person year (MD=0.61, 95% CI: -0.24, 1.46), and serious injurious falls per person year (MD=0.24, 95% CI: -0.24, 0.72). However, Campbell 2005<sup>38</sup> reported home safety modification reduced falls (incidence rate ratio [IRR]=0.39, 95% CI: 0.24, 0.62) and injurious falls at 12 months (IRR=0.56, 95% CI: 0.36, 0.87). The certainty of evidence was low, degraded for risk of bias (-1) and imprecision (-1).

#### Fear of falling and quality of life (1 trial, 28 participants)

In Waterman 2016,<sup>37</sup> the mean score at 6 months was not significantly different between groups in SFES-I (MD=2.55 scores, 95% CI: -0.51, 5.61) and SF-12 (MD=-3.14 scores, 95% CI: -10.86, 4.58). The certainty of evidence was low, downgraded for risk of bias (-1) and imprecision (-1).

### *2. Behavioral intervention versus social/home visits comparison (5 trials)*

#### Physical activity and falls (4 trials, 415 participants)

One trial assessed self-reported activity (Phone-FITT) at 3 months and 6 months (Figure 4).<sup>39</sup> There was no evidence that physical activity differed between a Falls Management Exercise program and usual activity at 3 months (MD=8 scores, 95% CI: -10.41, 26.41) and 6 months (MD=9.1 scores, 95% CI: -13.85, 32.5). The certainty of evidence was low, downgraded for risk of bias (-1) and imprecision (-1).

Three trials evaluated the outcomes of falls at 6 months and/or 12 months using various measurement methods.<sup>38,40,42</sup> Kovacs 2012<sup>42</sup> reported no significant difference between the Otago exercise program in addition to a standard osteoporosis exercise program compared with the standard osteoporosis exercise program alone when evaluating the proportion of fallers at 6 months (RR=0.54, 95% CI: 0.29, 1.01) and mean length of time to first fall (MD=3.7, 95% CI: -1.12, 8.52). In Campbell 2005<sup>38</sup>, no difference in falls (IRR=0.79, 95% CI: 0.48, 1.28) and injurious falls (IRR=0.82, 95% CI: 0.48, 1.40) at 12 months were found by comparing Otago exercise program plus vitamin D supplementation with social visits. Likewise, in Gleeson 2017<sup>40</sup>, no difference in falls (IRR=0.67, 95% CI: 0.36, 1.26) and injurious falls (IRR=0.49, 95% CI: 0.22, 1.11) at 12 months were reported by comparing Alexander technique with usual care. The certainty of evidence was low, downgraded for risk of bias (-1) and imprecision (-1).

#### Fear of falling and quality of life (3 trials, 190 participants)

Three trials assessed fear of falling scores at 3 to 12 months (Figure 4). Adams 2018<sup>39</sup> found the Falls Management Exercise program did not improve fear of falling compared with usual activity, using SFES-I scores at 3 months (MD=1 score, 95% CI: -0.13, 2.13) and 6 months (MD=0, 95% CI: -1.51, 1.51). Gleeson 2017<sup>40</sup> reported Alexander technique did not change SFES-I scores compared with usual care at 3 months (MD=-0.88 score, 95% CI: -2.72, 0.96) and 12 months (MD=-0.23 score, 95% CI: -2.08, 1.62). Likewise, in Jeter 2015,<sup>41</sup> no significant difference was observed in Illinois Fear of Falling score at 2 months by comparing Ashtanga-based Yoga therapy and usual activity. Jeter 2015<sup>41</sup> did not report the mean or median (i.e., the method of aggregation). The certainty of evidence was low, downgraded for risk of bias (-1) and imprecision (-1).

One trial investigated European Quality of Life-15 at 3 and 6 months.<sup>39</sup> This trial reported the Falls Management Exercise program improved quality of life at 6 months (MD=-0.15 score, 95% CI: -0.29, -0.01), but not at 3 months (MD=-0.08 score, 95% CI: -0.21, 0.05). The certainty of evidence was low, downgraded for risk of bias (-1) and imprecision (-1).

One trial assessed Geriatric Depression Scale (GDS-5) and Positive and Negative Affect Scale (PANAS) at 3 and 12 months.<sup>38</sup> No difference was noted by comparing the Otago exercise program with usual care for GDS-5 and PANAS.

### *3. Environmental intervention versus behavioral comparison (1 trial)*

#### Falls (1 trial, 197 participants)

One trial compared home safety modification with Otago exercise program on fall prevention at 12 months (Figure 5).<sup>38</sup> This trial found home safety modification reduced injurious falls (RR=0.66, 95% CI: 0.48, 0.91), but not all falls (RR=0.74, 95% CI: 0.53, 1.02).

### *4. Environmental and behavioral intervention versus social/home visits comparison (2 trials)*

#### Physical activity and falls (2 trials, 222 participants)

One trial compared home hazards modification and the Otago exercise program with social/home visits on measurements of physical activity at 6 months (Figure 6).<sup>37</sup> There were no significant differences in step counts (MD=-1073, 95% CI: -2577, 4231), walking time in minutes (MD=-13.15, 95% CI: -31.18, 4.18) or self-reported activity (MD=-5.36 scores, 95% CI: -16.01, 5.29).

Two trials assessed different measures of falls at 6 and 12 months. Waterman 2016<sup>37</sup> found no significant difference between groups at 6 months using proportion of fallers (RR=0.97, 95% CI:

0.54, 1.77), falls rate per person year (MD=0.64, 95% CI: -0.80, 2.08), moderate injurious falls per person year (MD=0.13, 95% CI: -0.55, 0.81), and serious injurious falls per person year (MD=0, 95% CI: -0.32, 0.32). Similarly, Campbell 2005<sup>38</sup> reported the home safety modification did not reduce falls (RR=0.78, 95% CI: 0.60, 1.01) and injurious falls at 12 months (RR=1.01, 95% CI: 0.81, 1.26) compared with Otago exercise program.

#### Fear of falling and quality of life (1 trial, 28 participants)

In Waterman 2016,<sup>37</sup> there was no significant difference between groups in mean score at 6 months using SFES-I (MD=1.12 scores, 95% CI: -1.05, 3.74) and SF-12 (MD=-2.82 scores, 95% CI: -10.39, 4.75) (Figure 6).

#### *5. Environmental and behavioral intervention versus environmental comparison (2 trials)*

##### Physical activity and falls (2 trials, 228 participants)

Waterman 2016<sup>37</sup> compared home hazards modification and the Otago exercise program with home hazard modification on measurements of physical activity at 6 months (Figure 7). There were no significant differences in step counts (MD=-1394, 95% CI: -3557, 779), walking time in minutes (MD=-15.20, 95% CI: -40.98, 10.58) or self-reported activity (MD=4.60 scores, 95% CI: -10.10, 19.30).

Two trials evaluated measures of falls at 6 and 12 months. Waterman 2016<sup>37</sup> found no significant difference between groups at 6 months using proportion of fallers (RR=0.78, 95% CI: 0.39, 1.54), falls rate per person year (MD=-0.1, 95% CI: -1.66, 1.46), moderate injurious falls per person year (MD=-0.48, 95% CI: -1.35, 0.39), and serious injurious falls per person year (MD=-0.24, 95% CI: -0.72, 0.24). Likewise, Campbell 2005<sup>38</sup> reported the home safety modification



with the Otago exercise program reduced injurious falls (RR=1.56, 95% CI: 1.17, 2.09), but not all falls at 12 months (RR=1.33, 95% CI: 0.95, 1.85).

#### Fear of falling and quality of life (1 trial, 30 participants)

In Waterman 2016,<sup>37</sup> there was no significant difference between groups in mean score at 6 months using SFES-I (MD=-1.43 scores, 95% CI: -5.15, 2.29) and SF-12 (MD=0.32 score, 95% CI: -6.02, 6.66) (Figure 7).

### *6. Environmental and behavioral intervention versus behavioral comparison (1 trial)*

#### Falls (1 trial, 195 participants)

One trial compared home safety modification and the Otago exercise program with Otago exercise program alone on measures of falls at 12 months (Figure 8).<sup>38</sup> This trial found no significant difference between groups using proportion of fallers (RR=0.99, 95% CI: 0.74, 1.32) and proportion of injurious fallers (RR=1.14, 95% CI: 0.90, 1.45).

## **Discussion**

### *Summary of main results*

This review included six RCTs of behavioral or environmental interventions in older people with vision impairment who met our eligibility criteria. We used both physical activity and falls as primary outcomes, because both measures are important physical domains in informing clinicians, patients, and other policy makers to make informed decisions.

The interpretation of the results for this review is complicated by the fact that environmental or behavioral interventions are not standard treatments, and often tailored individually and vary by severity of vision loss. Trial investigators reported physical activity and falls in many different ways that precluded any meta-analysis.

There is no evidence of effect for most of the environmental or behavioral interventions studied for reducing physical activity limitation and preventing falls in visually impaired older people.

We found low certainty of evidence that the environmental interventions, particularly home safety modification delivered by occupational therapists, may provide a small benefit on preventing falls compared with social/home visits; but did not appear to affect physical activity.

No evidence of benefit was found with diverse types of behavioral interventions on reducing activity limitation and preventing falls, and the certainty of evidence was generally low.

#### *Overall completeness and applicability of evidence*

The six RCTs in this review included 686 older people (mean age=80) with visual impairment, predominately women (69%). Participants characteristics varied due to enrolment method and inclusion criteria. Some trials generally recruited slightly younger people (median age=59) or those with less severe vision loss. In other trials, participants were more representative of older people with vision impairment living in the community. Some trials recruited people through low vision clinics, or with specific eye diseases such as age-related macular degeneration. Some trials excluded participants with neurological disorders or who were unable to walk in their own residence, so that the results may not be applicable to older people with cognitive impairment or living in dependency. The included trials were conducted in five countries with different health care systems; therefore, the effectiveness of interventions could be sensitive to a variety of

healthcare structures and networks settings. The results of this review should be interpreted with caution because four trials had low power to detect effect due to small sample size.<sup>39,41,42</sup>

This review identified a variety of interventions for behavioral treatment, which precludes exploring a broad effect of different components as a whole, such as differences between the Fall Management Exercise program and Otago program for example. Additionally, usual care in these included studies was "no intervention but retaining access to normal health and vision care"; however, standardization of comparator group would make it easier to consider for future meta-analysis. We sought fall-related measures including proportion of fallers, proportion of injurious fallers, falls rate per person year, injurious falls rate per person year, and mean length of time to first fall. Fall measures using both number of fallers and number of times a faller falls have clinical implications, because interventions may not prevent an individual from becoming a faller, but might prolong the time free from falls. Given the complexity of environmental and behavioral interventions and relatively small size of the six trials in this review, we cannot establish the applicability of the heterogeneous evidence in different settings and we do not know whether any benefits exist.

### *Quality of the evidence*

The overall certainty of evidence showing the effectiveness of environmental and behavioral intervention is low with methodological limitations. We downgraded the results by two levels, because the trials were judged as having a high risk of bias for at least one domain; the fall-related measures were inconsistent across trials; or small sample size for each comparison; and few events resulted in wide confidence interval crossing the line of no effect.

A major problem with the current evidence is that few of these trials measured widely agreed-upon outcomes with long follow-ups (12 months or more).<sup>34</sup> Additionally, limitations of the evidence were reflected from clinical heterogeneity of the six trials, including demographic characteristics of participants (e.g., age, sex, and country of residence) and clinical characteristics (e.g., causes and severity of vision impairment and other comorbidities). Such clinical heterogeneity made it problematic to combine the effect estimates from individual trials to evaluate the overall effect in meta-analyses.

#### *Potential biases in the review process*

We attempted to minimize bias by having two review authors independently review the titles and abstracts. We deliberately did not narrow our population and included both community-dwelling and care home/residential older adults, so we believe we included all evidence that applied to the population group of interest. It was possible that we were too precise in our interventions by excluding, for example, computerized visual field or eccentric view training, but the focus of this review was to consider modifications to the home environment, and coping and enabling strategies to navigate safely in and out of the home. In addition, it was difficult to identify studies that measured but did not report the outcomes (i.e., physical activity or falls); however, this was unlikely to bias our study as they were not reported, and we provided the reason for exclusion as "outcome of interest not measured."

#### *Agreements and disagreements with other studies or reviews*

The Cochrane review<sup>21</sup> considered the effectiveness of Orientation and Mobility training in adults with low vision. The review included two small trials comparing Orientation and Mobility

training to physical exercise with weak evidence. Orientation and Mobility training had no effect in one study while it was found to be beneficial in the second. There is therefore little evidence on which type of Orientation and Mobility training is better for people with low vision who have specific characteristics and needs. This review is not specific to older adults with visual impairment.

Work commissioned by the Thomas Pocklington Trust<sup>47</sup> aimed to carry out a qualitative evidence synthesis of qualitative research exploring the views and experiences of older people with visual impairment on participation in falls prevention initiatives. However, no studies were found which explicitly sought to explore the views of older visually impaired people, and three studies were included as all had relevant data which could be considered. The single theme extending across all three studies was the capacity and desire for autonomous decision-making around environmental modification by older people with visual impairment, informed by but not dependent on the recommendations of others such as health professionals. Other themes elicited included: the influence of function, ambience, safety, cleanliness and use of cues in decision-making about environmental modification. This research<sup>47</sup> drew summaries based on the original version of this review.<sup>31</sup>

Although there are previous systematic reviews of the effect of interventions to reduce falls in older adults,<sup>26,27,48</sup> there is no specific review of those with visual impairment. However, one Cochrane Review<sup>49</sup> did show that home safety interventions were more effective in reducing rate of falls and risk of falls in the higher risk subgroup of older people. They also found that there was some evidence that occupational therapy-led interventions on home safety assessment were more effective than non-occupational therapy-led interventions for reducing rate of falls, but this

review was not performed on visually impaired people. Additionally, a recent review assessed the effectiveness of low vision rehabilitation on health-related quality of life and vision-related quality of life in visually impaired people,<sup>32</sup> but this review was not conducted on older adults (aged 60 or older). In van Nispen 2020,<sup>32</sup> no evidence of benefit was reported for various types of low vision rehabilitation interventions on health-related quality of life, although the authors found low and moderate-certainty evidence of benefit by comparing psychological therapies versus usual care for vision-related quality of life. Most of the included studies in van Nispen 2020<sup>32</sup> on low vision rehabilitation had a short follow-up (6 months or less).

A systematic review<sup>50</sup> reminds researchers that outcome measures chosen to determine the effectiveness of low vision services should reflect capacity within daily activities, within the home environment, rather than just on clinical outcomes. This review only found seven trials, and whilst they felt able to confirm that rehabilitation services resulted in improved clinical and functional outcomes, they commented that the number of studies meeting their inclusion criteria was ‘pitifully small’. Indeed, there is growing interest in physical activity in those living with low vision, as reflected by the advent of wearable technology, which has created unprecedented opportunity to monitor real-world activity objectively that is often overlooked by questionnaires.<sup>51,52</sup> Future trials investigating whether interventions can make a difference to habitual activity should consider both objective and subjective assessments of physical activity.

## **Authors' conclusions**

### *Implications for practice*

There is no evidence of effect for most of the environmental or behavioral interventions studied for reducing physical activity limitation and preventing falls in visually impaired older people. However, the fact that we have been unable to show the evidence of effect does not mean there is no effect, merely that there are only six eligible studies addressing this issue and these studies cannot be combined in meaningful ways.

Although behavioral interventions delivered by occupational therapists may reduce the rate of falls, we are unable to conclude if this is due to reduced activity restriction (increased mobility) or reduced activity (lessening exposure to risk). There are also limited and inconclusive results arising from the evaluation of environmental and behavioral interventions aimed at improving quality of life.<sup>53</sup> This is perhaps because these intervention studies have not focused on coping strategies to engage with leisure activities and have instead focused on essential activities of daily living.

As restricted activity can lead to declining mobility, to potential distress and anxiety, and to an increased risk of falls, healthcare professionals need to consider ways to facilitate people to increase physical activity and prevent falls in older people with visual impairment.

### **Implications for research**

There is a gap in knowledge concerning the effectiveness of environmental and behavioral interventions in reducing activity restriction and preventing falls in older people with irreversible vision loss. Future research, such as the ongoing trial described in Zijlstra 2009,<sup>22</sup> considering the effectiveness of orientation and mobility training on activity restriction, physical activity, falls, fear of falling and quality of life in older adults with low vision, is necessary before any

conclusions can be reached. Moreover, the physical activity program delivering through the telerehabilitation that enables remote prescription and monitoring of exercise may be considered as a feasible and safe technology for visually impaired people in future studies.<sup>54</sup>

Of final note is the concern that interventions are rarely described in detail,<sup>55</sup> nor do they provide information on the most appropriate participant groups or types of visual impairment with which they are most effective. It is important to customize interventions to suit particular individuals and their needs and preferences. A 'black box' of multiple interventions makes it difficult to pull out the effectiveness of different parts of the interventions, e.g. a mix of environmental and behavioral interventions may make it difficult to disentangle which type of intervention is more appropriate for which participant group.

## **Acknowledgements**

The review authors would like to acknowledge the Cochrane Eyes and Vision (CEV), in particular, Iris Gordon for compiling the search strategy and searches.

Dr. Tianjing Li (PI for CEV US satellite) was funded by UG1 EY020522 from the National Institutes of Health.

The views expressed in this publication are those of the authors and not necessarily those of the NIHR, NHS, NIH or the Department of Health.

This 2020 review update was managed by CEV@US and was signed off for publication by Tianjing Li and Richard Wormald.

## **Contributions of authors**



*Authors contributing to this update review:*

Conceiving the update review: JE, DS, TL

Designing the update review: JE, DS, TL

Screening search results: JE, US, LM, KT, LG, TH

Extracting data: JE, DS, KT, TH

Writing the first draft: JE, DS

Revising the review: JE, DS, TL

Commenting on the review: JE, DS, TL, US, LM, KT, LG, TH

### **Previous version of the review**

Skelton, Ballinger, Neil and Howe conceived and developed the protocol. Gray and Palmer commented on drafts of the protocol and search strategies. Skelton and Howe reviewed all selected publications, with Gray as adjudicator. Ballinger, Howe, Palmer and Gray commented on drafts of the review.

### **Declarations of interest**

DS is a Director of Later Life Training Ltd, a not for profit training company in the UK that delivers training to health and fitness professionals in delivery of the Fall Management Exercise and Otago exercise programs.

## **Differences between protocol and review**

The title and objectives have been changed from previous version of this review. "Preventing falls" was added into the title. The population qualifier "*community-dwelling*" has been removed from the title of this review since the last version was published, but the inclusion criteria with respect to the study population have not changed, i.e., we included older people living independently and those living in residential settings.

Falls have been changed from secondary to primary outcome of this review because there is no specific review to study effect of environmental and behavioral interventions to reduce falls in visually impaired older adults, and reducing physical activity limitation is deemed as one outcome for fall prevention trials. To be eligible for inclusion in this update, the included studies had to report physical activity and/or fall-related measures.

## Characteristics of studies

### *Characteristics of included studies*

Adams 2018

Methods	<p>Study design: RCT</p> <p>Number randomized: 64 (33 in the intervention group; 31 in the usual activity group)</p> <p>Number analyzed: 64</p> <p>Number of centers: 2</p> <p>Date of first enrollment: January 2015</p> <p>Length of follow-up: 24 weeks</p> <p>Sample size estimation: the authors aimed to recruit a total of 80 community-living visually impaired older adults to allow for loss to follow-up.</p>
Participants	<p>Country: UK</p> <p>Age: mean 78 years (range 61 to 95 years)</p> <p>Sex: 39% male, 61% female</p> <p>Key inclusion criteria: having visual impairment, living in own home, walking independently, physically being able to participant in exercise class</p> <p>Key exclusion criteria: unable to understand instructions in English, uncontrolled medical diseases, having conditions requiring a specialist exercise program, unable to maintain upright position, no indoor mobility, included in other fall prevention programs</p> <p>Comparability of baseline characteristics: comparable</p>
Interventions	<p>Behavioral intervention #1: the exercise program (Falls Management Exercise) consisted of one hour weekly sessions over 12 weeks and was held in community venues with a maximum capacity of ten participants per group. The exercises consisted of balance specific, individually-tailored and targeted training for dynamic balance, strength, endurance, flexibility, gait and functional skills, training to improve 'righting' or 'correcting' skills to avoid a fall and backward-chaining i.e. retraining of the ability to get down to and up from the floor. Functional floor exercises and adapted Tai Chi exercises were also carried out with progressively more challenging content over the 12 weeks. Resistance bands and mats were used. Participants were also advised to exercise at home for up to two hours per week. The exercises were to be performed if possible daily, on the days the participant was not attending the exercise class. All home programs contained 'prompts' that linked exercises to daily tasks e.g. performing heel raises whilst waiting for the kettle to boil, in order to improve adherence. Exercises were provided in a large text booklet, DVD or audio format. Exercises were designed to be completed in 10 to 20min blocks, become more challenging and graduate into longer periods.</p> <p>Control intervention #2: participants received no intervention and continued with their usual activities. They were offered an equivalent exercise program after the 24 weeks follow-up.</p>

Outcomes	<p>Primary outcome: fear of falling scores at 24 weeks measured by The Short Falls Efficacy Scale - International (SFES-I).</p> <p>Secondary outcomes: (1) physical activity (self-reported physical activity questionnaire [Phone-FITT]), (2) health-related quality of life (European Quality of Life 15), (3) activity avoidance, (4) time Get Up &amp; Go test, (5) falls risks (Falls Risk Assessment Tool), (6) loneliness (Six-Item Scale for Overall, Emotional, and Social Loneliness), (7) Home Anxiety and Depression Scale (14 items), (8) Work and Social Adjustment Scale.</p>
Notes	<p>Funding sources: Public Health Research Program of the National Institute for Health Research (NIHR), Health Promotion Interventions for People with Impairment Program, UK</p> <p>Statistical analyses: appropriate</p> <p>Subgroup analyses: none reported</p> <p>Registration: ISRCTN ID: 16949845</p>

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomization was stratified by center and was administered centrally via Newcastle Clinical Trials Unit using a secure web based system using a blocked allocation system to allocate participants to the two groups.
Allocation concealment (selection bias)	Low risk	A blocked allocation (permuted random blocks of variable length) system was used to allocate participants to the two groups (block size will not be disclosed to the investigators) in a 1:1 ratio to intervention and control groups. Participant screening ID, initials and gender were entered into the web-based system, which would return the allocation status. Participants were informed by telephone, of their allocated treatment group following randomization.
Blinding of participants and personnel (performance bias)	High risk	Participants were informed of their allocated treatment group following randomization.
Blinding of outcome assessment (detection bias)	Unclear	Insufficient information to assess.
Incomplete outcome data (attrition bias)	Low risk	49 out of 64 (92%) participants completed the 24-week visit (four had withdrawn completely and one was lost to follow up from the study). In two cases, assessments were completed outside the two-week limit, due to other commitments or extenuating circumstances. All participants in the intervention group remaining in the trial at each time point completed each of the questionnaires. There were two occasions when participants in the usual activity group

		partially completed a questionnaire, and two occasions on which whole questionnaires were not completed.
Selective reporting (reporting bias)	High risk	Not all outcomes reported: i.e., activity avoidance, and loneliness.
Other bias	Low risk	No other sources of bias identified.

#### Campbell 2005

Methods	<p>Study design: RCT</p> <p>Number randomized: 391 (100 in environmental group, 97 in behavioral group, 98 in the environmental and behavioral group, 96 in the social visit group)</p> <p>Number analyzed: 391</p> <p>Number of centers: 2</p> <p>Date of first enrollment: January 2002</p> <p>Length of follow-up: 12 months</p> <p>Sample size estimation: the authors used the rate of falls in those aged <math>\geq 75</math>, 35% reduction in falls achieved, a power of 0.80, and a two sided significance of 0.05. The authors allowed for the Poisson distribution of falls and a 20% dropout rate.</p>
Participants	<p>Country: New Zealand</p> <p>Age: mean 84 years (range 75 to 96 years)</p> <p>Sex: 32% male, 68% female</p> <p>Key inclusion criteria: having poor vision (visual acuity of 6/24 or worse in the better eye after the best possible correction), and living in the community.</p> <p>Key exclusion criteria: unable to walk around their own residence, receiving physiotherapy at time of enrollment, could not understand the study requirement</p> <p>Comparability of baseline characteristics: comparable</p>
Interventions	<p><u>Environmental intervention #1</u>: occupational therapists visited the person at home and assessed home safety using a checklist. They identified hazards and initiated a discussion with the participant about any items that could lead to falls. The therapists and participant agreed on which recommendations to implement. The therapists listed these recommendations in a follow-up letter to the participant. They facilitated provision of equipment and payment from usual sources depending on the price and type of the home modification. Referrals were made to the Royal New Zealand Foundation of the Blind. A second home visit was needed to sign off the equipment installed by some providers.</p> <p><u>Behavioral intervention #2</u>: physiotherapists initiated a one-year Otago exercise program (specific muscle strengthening and balance retraining exercises). It was modified for those with severe visual acuity loss, and with vitamin D supplementation. The physiotherapists prescribed the exercises during five home visits at weeks one, two, four, and eight and a booster visit after six months. The degree of difficulty of the exercise and the number of 1, 2, and 3kg ankle cuff weights were used for muscle strengthening and increased at each visit as appropriate. Audio tapes of the exercises in four</p>

	<p>different levels of difficulty were available for those who could not see the exercise instruction sheets. Participants were expected to exercise at least three times a week (about 30 minutes a session) and to walk. The physiotherapists delivered vitamin D tablets if needed. For the months with no scheduled home visit, the physiotherapists telephoned to encourage the person to maintain motivation and discuss any problems.</p> <p><u>Environmental and behavioral intervention #3</u>: received both the environmental and behavioral intervention.</p> <p><u>Control intervention #4</u>: research staff made two home visits lasting an hour each during the first six months of the trial to participants who were not randomized to either environmental or behavioral intervention groups.</p>
Outcomes	<p>Primary outcome: number of fallers at 12 months</p> <p>Secondary outcomes: (1) falls per person year, (2) number of injurious falls, (3) injurious falls per person year, (4) incidence rate ratio for falls, (5) incidence rate ratio for injurious falls, (6) costs of implementing environmental intervention</p>
Notes	<p>Funding sources: Health Research Council of New Zealand</p> <p>Statistical analyses: appropriate</p> <p>Subgroup analyses: reported</p> <p>Registration: ISRCTN ID: 15342873</p>

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A statistician developed the group allocation schedule using computer generated random numbers
Allocation concealment (selection bias)	Low risk	The schedule was held by an independent person at a separate site and was accessed by a research administrator for the study, who telephoned after each baseline assessment was completed
Blinding of participants and personnel (performance bias)	High risk	Participants were informed of their allocated treatment group following randomization.
Blinding of outcome assessment (detection bias)	Low risk	Falls were monitored for one year for each person using prepaid, addressed, tear-off monthly postcard calendars. The independent assessors in each center telephoned participants to record the circumstances of the falls and any resulting injuries or use of resources. They remained blind to group allocation.
Incomplete outcome data (attrition bias)	Low risk	361 out of 391 (92%) participants completed one year of follow-up. The mean and total follow-up time were equal by four arms. Reasons for not being follow-up were reported and similar across four arms.

Selective reporting (reporting bias)	Low risk	Outcomes specified in the study protocol were reported.
Other bias	Low risk	No other sources of bias identified.

#### Gleeson 2017

Methods	<p>Study design: RCT</p> <p>Number randomized: 120 (60 in the intervention group; 60 in the usual activity group)</p> <p>Number analyzed: 120</p> <p>Number of centers: 1</p> <p>Date of first enrollment: August 2010</p> <p>Length of follow-up: 3 months</p> <p>Sample size estimation: the study was powered to measure the impact of the Alexander technique on physical function such that 60 individuals in each of the two groups (N=120) would give the study 80% power to detect a 15% between-group difference at a 5% level of significance allowing for 15% drop-outs during the 12 months for the primary outcome.</p>
Participants	<p>Country: Australia</p> <p>Age: mean 75 years (SD=10)</p> <p>Sex: 29% male, 71% female</p> <p>Key inclusion criteria: having a vision impairment, having had an orientation and mobility program from Guide Dogs within last five years, living within Sydney metropolitan area, not need an interpreter</p> <p>Key exclusion criteria: not reported</p> <p>Comparability of baseline characteristics: comparable</p>
Interventions	<p><u>Behavioral intervention #1</u>: participants received 12 lessons (30 mins long) for Alexander technique in individual one on one sessions in the participant's own home. The Alexander technique was a physical conditioning program designed to alter and improve the way individuals move and react to physical stimuli. A typical session included completing activities of daily living, while being assisted by a trained Alexander technique practitioner. The completion of these activities was accompanied by psychological techniques including mindfulness, co-ordination and body-mapping. The exercises were designed to improve postural stability, co-ordination and confidence during movement. A lesson protocol was developed using everyday activities such as movements between sitting and standing, getting to and from the floor, and walking, climbing stairs and conducting everyday activities. Subsequent lessons were based on prior progress, and the lesson plan was modified as necessary. The Alexander Technique lessons were delivered by one person who was an accredited teacher of the Alexander Technique.</p> <p><u>Control intervention #2</u>: participants received usual care (able to access orientation and mobility programs) from Guide Dogs.</p>
Outcomes	<p>Primary outcome: physical performance from the Short Physical Performance Battery at 12 months</p> <p>Secondary outcomes: (1) number of falls, (2) falls rate per person, (3) fear of falling scores by the Short Falls Efficacy Scale - International (SFES-I), (4)</p>

	mood with the Geriatric Depression Scale-5 (GDS-5) and the Positive and Negative Affect Scale (PANAS), (5) The Perceived Visual Ability Scale, (6) The Keele Assessment of Participation
Notes	Funding sources: Guide Dogs NSW/ACT, Sydney, Australia; The Australian Society of Teachers of the Alexander Technique, Beechworth, Victoria; and the FM Alexander Trust, London, UK Statistical analyses: appropriate Subgroup analyses: reported Registration: ACTRN12610000634077

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A block randomized (block permutation size 1, 2 and 4) sequence using a computer generated list.
Allocation concealment (selection bias)	Low risk	The computer generated list was kept by a separate center-based investigator who had no contact with the participants.
Blinding of participants and personnel (performance bias)	High risk	The participants and the intervention providers could not be masked to group allocation.
Blinding of outcome assessment (detection bias)	Low risk	All outcome assessors remained masked to group allocation for all assessments, and participants were asked not to reveal their allocation status.
Incomplete outcome data (attrition bias)	Unclear	Of the 120 participants who entered the study, 10 did not complete all assessments. Data not reported for these people. Since 92% participants were followed up, we judged it as unclear risk of bias.
Selective reporting (reporting bias)	Low risk	Outcomes specified in the study protocol were reported.
Other bias	Low risk	No other sources of bias identified.

Jeter 2015

Methods	Study design: RCT Number randomized: 21 (11 in the intervention group; 10 in the usual activity group) Number analyzed: 17 Number of centers: 1 Date of first enrollment: October 2012 Length of follow-up: 8 weeks Sample size estimation: the author reported a sample size calculation was not applicable to this type of exploratory study; however, a minimum of 10 subjects per group was feasible to provide an indication of the acceptability.
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Participants	<p>Country: US</p> <p>Age: median 59 years (range: 27 to 85 years)</p> <p>Sex: 35% male, 65% female</p> <p>Key inclusion criteria: blindness (best-corrected visual acuity worse than 20/200 and/or visual field less than 20° in diameter in the better eye), ocular diseases that were stable throughout 3-6 months, able to participate in yoga program, English-speaking</p> <p>Key exclusion criteria: individuals with vestibular disorders, acute orthopedic problems that affect ambulation, history of neurologic disease (e.g., peripheral neuropathy), or who were pregnant or taking medication that could affect balance (e.g., sleeping pills)</p> <p>Comparability of baseline characteristics: comparable</p>
Interventions	<p><u>Behavioral intervention #1:</u> Ashtanga-based Yoga Therapy (AYT) for 8 weeks. One group session per week with the instructor and an experienced yoga assistant. Participants were provided with a free yoga mat and an audio CD developed by the author to practice at home and were asked to practice at least twice a week (i.e. equivalent to approximately 16 home practice sessions during the intervention period). The AYT is amenable to study because it is composed of a standardized sequence of postures held for a fixed duration. Each pose was held for five breaths or for as long as the subject was able.</p> <p><u>Control intervention #2:</u> waitlist group with no active intervention.</p>
Outcomes	<p>Primary outcome: center of pressure at 8 weeks, stability index at 8 weeks</p> <p>Secondary outcomes: (1) timed one-leg stance, (2) physical function, (3) Illinois fear of falling scores (only p-value reported).</p>
Notes	<p>Funding sources: Louise L. Sloan Research Grant Award, Lions Vision Research Foundation, Wilmer Eye Institute, Johns Hopkins University (\$2,000) and National Eye Institute, Diversity Supplement.</p> <p>Statistical analyses: appropriate</p> <p>Subgroup analyses: not reported</p> <p>Registration: NCT01366677</p>

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomization to group assignment was conducted by the study PI using the random number generator in MATLAB (Mathworks, Inc.).
Allocation concealment (selection bias)	Low risk	A research assistant assigned unidentifiable subject IDs (i.e. #1–21) to subjects after enrollment.
Blinding of participants and personnel (performance bias)	High risk	Masking participants to the yoga intervention was not possible.
Blinding of outcome	Low risk	Trained research assistants were masked to the group assignment during data collection.

assessment (detection bias)		
Incomplete outcome data (attrition bias)	Low risk	17 out of 21 (81%) participants completed 8-week of follow-up. Two participants in each arm were not follow-up, and reasons for not being follow-up were reported and similar.
Selective reporting (reporting bias)	High risk	The data represented the quantitative results are subset of a larger battery of assessments that included psychological questionnaires and other qualitative information
Other bias	Low risk	No other sources of bias identified.

#### Kovacs 2012

Methods	<p>Study design: RCT</p> <p>Number randomized: 41 (21 in the intervention group; 20 in the usual activity group)</p> <p>Number analyzed: 41</p> <p>Number of centers: 1</p> <p>Date of first enrollment: February 2010</p> <p>Length of follow-up: 8 weeks</p> <p>Sample size estimation: the author reported this study had small sample size which reduced the statistical power of their analyses. Based on their results, a post hoc power analysis indicated that at least 171 participants in each group would require to achieve a statistical power of 80%.</p>
Participants	<p>Country: Hungary</p> <p>Age: mean 70 years (SD: 7 years)</p> <p>Sex: 100% female</p> <p>Key inclusion criteria: living in nursing homes with age-related visual impairment, being female.</p> <p>Key exclusion criteria: being totally blind, had lived in the nursing home for less than 2 months, being unable to walk around their own residence, progressively being unable to walk around their own residence, progressively increasing severity of neurological, and unstable cardiovascular diseases that would limit participation in exercise program, planned moving away from the nursing home during the study period and participated in an exercise program including balance exercise within 6 months</p> <p>Comparability of baseline characteristics: comparable</p>
Interventions	<p>Behavioral intervention #1: participants joined twice a week in a multimodal exercise program for 30 min and twice a week in the standard osteoporosis exercise program. The multimodal exercise program included balance and strength exercises based on Otago Exercise Program.</p> <p>Control intervention #2: participants joined in the standard osteoporosis exercise program alone for four times a week in 30 min.</p>
Outcomes	<p>Primary outcome: Berg Balance Scale at 6 months,</p> <p>Secondary outcomes: (1) Timed Up and Go, (2) Barthel activity of daily living, (3) number of fallers, (4) mean length of time to first fall in weeks.</p>
Notes	Funding sources: the study was not sponsored

	Statistical analyses: appropriate Subgroup analyses: not reported Registration: not available
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#### Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Blocked randomization was performed (with a block size of 4).
Allocation concealment (selection bias)	Low risk	Assignment was numbered opaque identical sealed envelopes. The envelopes were prepared by an independent physiotherapist.
Blinding of participants and personnel (performance bias)	High risk	Therapist and participants were not blinded to group allocation.
Blinding of outcome assessment (detection bias)	Low risk	The outcome assessor was uninformed about group allocation and was not involved in proceedings of the exercise programs. Participants were asked not to reveal details of their treatment to the outcome assessor.
Incomplete outcome data (attrition bias)	Low risk	All participants completed 8-week of follow-up. No participants were excluded from the study.
Selective reporting (reporting bias)	Low risk	Outcomes specified in the study protocol were reported
Other bias	Low risk	No other sources of bias identified

#### Waterman 2016

Methods	Study design: RCT Number randomized: 49 (16 in environmental group; 17 in environmental and behavior group, 16 in the control group) Number analyzed: 43 Number of centers: 1 Date of first enrollment: July 2011 Length of follow-up: 6 months Sample size estimation: the author reported the intended sample size was 30 participants in each group (a simple randomization 1:1:1 ratio) allowing for 10 % attrition rate.
Participants	Country: UK Age: mean 81 years (SD: 8 years) Sex: 35% male, 65% female Key inclusion criteria: having a vision impairment (Binocular visual acuity >0.6 LogMAR, and/or moderate visual field loss defined as affecting more than 20% of the test locations used in a binocular Esterman test), living

	<p>independently in community, being able to walk around own residence, cognitively able to participate and understand study requirements.</p> <p>Key exclusion criteria: receiving an OT or physiotherapist intervention or home safety assessment and modification or exercise intervention, including attendance at a Falls Clinic, not achieving between 7 and 10 on the Abbreviated Mental Test.</p> <p>Comparability of baseline characteristics: comparable</p>
Interventions	<p>Environmental intervention #1: participants received the Home Safety (HS) program implemented by an Occupational Therapist (OT). An experienced trained OT used an amended version of the Westmead Home Safety Assessment to discuss environmental hazards present in their homes with participants. This resulted in a jointly agreed action plan incorporating participant needs and views. The action plan focused on how the participant could alter their environment to reduce the likelihood of falls.</p> <p>Environmental and behavioral intervention #2: participants received the HS plus the home exercise program both implemented by the OT and supported by a volunteer peer mentor. The HS was described above, the home exercise included the Otago Exercise Program (OEP) for 6 months. The exercises, stressing both strength and balance, were individually prescribed, progress in difficulty, and were undertaken for 30 min at least three times per week. A walking plan was also agreed with all participants to be undertaken at least twice per week.</p> <p>Control intervention #3: usual care from the NHS, but in addition received three social visits and two telephone calls by lay visitors (volunteer student nurses, alumni and members of staff from the university)</p>
Outcomes	<p>Primary outcome: number of falls at 6 months, number of injurious falls at 6 months.</p> <p>Secondary outcomes: (1) adherence rate, (2) self-reported physical activity questionnaire (Phone-FITT), (3) objective measures of physical activity (activPALTM activity monitor): daily step counts and walking time (minutes) (4) quality of life (12-Item Short Form Health Survey), (5) visual disability (Vision-Related Quality of Life), (6) Attitudes to Falls-Related Interventions Scale, (7) Fear of Falling (SFES-I).</p>
Notes	<p>Funding sources: National Institute for Health Research (NIHR) under the Research for Patient Benefit Program (RfPB), reference number: PB-PG-0909-20090.</p> <p>Statistical analyses: appropriate</p> <p>Subgroup analyses: not reported</p> <p>Registration: ISRCTN53433311</p>

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Participants were then independently randomized by the Clinical Trials Unit via a web-based secure randomization

		service, which informed the Occupational Therapist or lay visitor coordinator of the group assignment
Allocation concealment (selection bias)	Low risk	Occupational Therapist and coordinator did not know the next assignment when implementing the randomization
Blinding of participants and personnel (performance bias)	High risk	Participants and the Occupational Therapist delivering the intervention, social visitors and Peer Mentors could not be blinded to group allocation.
Blinding of outcome assessment (detection bias)	Low risk	The research assistant and statistician were blinded to group allocation
Incomplete outcome data (attrition bias)	Low risk	43 out of 49 (88%) participants completed 6-month of follow-up. Number of participants with follow-up were equal between groups. No missing outcome data. Participants were phoned to ensure complete data set.
Selective reporting (reporting bias)	Low risk	Outcomes specified in the study protocol were reported
Other bias	Low risk	No other sources of bias identified

#### Footnotes

FaME: Falls Management Exercise

Phone-FITT: Telephone questionnaire for self-report of physical activity

SFES-I: Short Falls Efficacy Scale-International

EuroQoL: European Quality of Life

PANAS: Positive and Negative Affect Scale

GDS-5: Geriatric Depression Scale-5

Ashtanga-based Yoga Therapy (AYT)

OT: Occupational Therapist

HS: Home Safety

OEP: Otago Exercise Programme

SF-12: 12-Item Short Form Health Survey

## Characteristics of ongoing studies

ACTRN12607000399493

Study name	A randomized controlled trial of a low vision self management program on quality of life in people with low vision.
Methods	Study design: RCT Number randomized: 240 (target) Number analyzed: not reported Number of centers: not reported Date of first enrollment: January 2007 Length of follow-up: 16 months Sample size estimation: not reported
Participants	Country: Australia Age: not reported Sex: not reported Key inclusion criteria: aged 55 or older, visual impairment (visual acuity of <6/12 and >6/480 in the better eye with habitual correction), English-speaking, no cognitive impairment, adequate hearing. Key exclusion criteria: not reported Comparability of baseline characteristics: not applicable
Interventions	Behavioral intervention #1: participants receive new low vision self-management program “Living with Low Vision”. It consist of eight 3-hour weekly facilitated group sessions. The program is structured and a facilitator manual clearly outline the content and delivery. As well as providing information, the topics in the program are covered by exploring participants' experiences, difficulties and solutions. Participants are encouraged to draw on their extensive life experience and coping mechanisms and to develop new skills and strategies and apply these new techniques in their daily life. Participants are given the option to bring a relative, friend or acre to the program with them. Control intervention #2: participants continue to access usual low vision rehabilitation services.
Outcomes	Primary outcome: Vision Impairment Questionnaire (IVI) to assess the restriction of participation in daily activities in people with low vision, the Depression Anxiety Stress Scale (DASS) to assess psychological well-being. Secondary outcomes: (1) Adaptation to Age-related Vision Loss Scale (AVL-12), (2) The General Self-Efficacy Scale (GSES), (3) The Health Education Impact Questionnaire (HEIQ) scale, (4) The Positive and Negative Affect Schedule (PANAS).
Starting date	1/03/2007
Contact information	Professor Jill Keeffe
Notes	The trial was recruiting participants, accessed on 01/31/2020, through: <a href="http://apps.who.int/trialsearch/Trial3.aspx?trialid=ACTRN12607000399493">http://apps.who.int/trialsearch/Trial3.aspx?trialid=ACTRN12607000399493</a> .

### Footnotes

IVI: Vision Impairment Questionnaire

DASS: Depression Anxiety Stress Scale

AVL-12: Adaptation to Age-related Vision Loss Scale

GSES: General Self-Efficacy Scale

HEIQ: Health Education Impact Questionnaire

PANAS: Positive and Negative Affect Scale

## Summary of findings tables

### 1 Summary of findings

1. Environmental intervention compared with social/home visits comparison for older adults with visual impairment					
Patient or population: older adults (aged 60 and over) with irreversible visual impairment					
Settings: living independently					
Intervention: home safety modification by occupational therapists					
Comparison: social/home visits, such as social support to discuss general topics about lifestyles without providing clinical advice					
Outcomes	Anticipated absolute effects* (95% CI)		Relative effects*	No of Participants (studies)	Quality of the evidence (GRADE)
	Risk with control	Risk with environmental intervention			
Physical activity at 6 months  Assessed with different measures (step counts, walking time, and self-reported physical activity)	1 trial reported no difference in mean estimates between groups. Step counts: MD=321 (95% CI, -1981, 2622); average walking time (minutes): MD=1.70 (95% CI, -24.03, 27.43); self-reported physical activity: MD=-3.68 scores (95% CI, -20.6, 13.24)			28 (1 RCT)	⊕⊕⊕⊖ low <sup>1</sup>
Fall measures  Assessed with different measures (proportion of fallers at 6 months)	8/13	7/15	RR=0.76, 95% CI, 0.38, 1.51	28 (1 RCTs)	⊕⊕⊕⊖ low <sup>2</sup>
Fear of falling scores at 6 months  Assessed by Short Falls Efficacy Scale-International	Mean fear of falling was 10.38 scores	Mean fear of falling was 12.93 scores	MD 2.55 scores higher (95% CI, 0.51 lower to 5.61 higher)	28 (1 RCT)	⊕⊕⊕⊖ low <sup>3</sup>
Quality of life at 6 months	Mean quality of life was	Mean quality of life was 42.89 scores	MD 3.14 scores lower (95% CI,	28 (1 RCT)	⊕⊕⊕⊖ low <sup>4</sup>



Assessed by 12-Item Short Form Health Survey	46.03 scores		10.86 lower to 4.58 higher)		
The relative effect of the intervention (and its 95% CI). CI: Confidence interval; MD: Mean Difference; RR: Risk Ratio.					
<p>GRADE Working Group grades of evidence</p> <p>High quality: We are very confident that the true effect lies close to that of the estimate of the effect.</p> <p>Moderate quality: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.</p> <p>Low quality: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.</p> <p>Very low quality: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.</p>					

### Footnotes

<sup>1</sup>Downgraded 1 level due to study limitations (high risk of performance bias) and 1 level due to imprecision (small sample size of n = 28)

<sup>2</sup>Downgraded 1 level due to study limitations (high risk of performance bias), and 1 level due to imprecision (small sample size of n = 28)

<sup>3</sup>Downgraded 1 level due to study limitations (high risk of performance bias) and 1 level due to imprecision (small sample size of n = 28)

<sup>4</sup>Downgraded 1 level due to study limitations (high risk of performance bias) and 1 level due to imprecision (small sample size of n = 28)

## 2 Summary of findings

2. Behavioral intervention compared with usual activity or social/home visits comparison for older adults with visual impairment					
Patient or population: older adults (aged 60 and over) with irreversible visual impairment					
Settings: living independently or in residential settings					
Intervention: behavioral rehabilitation, such as falls management exercises programs, Otago exercise program, Alexander technique, Ashtanga-based Yoga therapy					
Comparison: usual activity or social/home visits, such as social support to discuss general topics about lifestyles without providing clinical advice					
Outcomes	Anticipated absolute effects* (95% CI)		Relative effects*	No of Participants (studies)	Quality of the evidence (GRADE)
	Risk with control	Risk with behavioral intervention			
Physical activity at 6 months  Assessed by self-reported physical activity	Mean self-reported physical activity was 43 scores	Mean self-reported physical activity was 52.1 scores	MD 9.1 scores higher (95% CI, -13.85 lower to 32.5 higher)	59 (1 RCT)	⊕⊕⊕⊖ low <sup>1</sup>
Fall measures  Assessed with different measures (proportion of fallers at 6 months)	14/20	8/21	RR=0.54, 95% CI, 0.29, 1.01	41 (1 RCT)	⊕⊕⊕⊖ low <sup>2</sup>
Fear of falling scores at 6 months  Assessed by Short Falls Efficacy Scale-International	Mean fear of falling was 8 scores	Mean fear of falling was 8 scores	MD 0 score (95% CI, -1.51 lower to 1.51 higher)	59 (1 RCT)	⊕⊕⊕⊖ low <sup>3</sup>
Quality of life at 6 months  Assessed by European Quality of Life-15	Mean quality of life was -0.06 score	Mean quality of life was -0.21 score	MD -0.15 score (95% CI, -0.29 lower to -0.01), not clinically different	59 (1 RCT)	⊕⊕⊕⊖ low <sup>4</sup>

<p>The relative effect of the intervention (and its 95% CI).</p> <p>CI: Confidence interval; MD: Mean Difference; RR: Risk Ratio.</p>
<p>GRADE Working Group grades of evidence</p> <p>High quality: We are very confident that the true effect lies close to that of the estimate of the effect.</p> <p>Moderate quality: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.</p> <p>Low quality: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.</p> <p>Very low quality: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.</p>

### Footnotes

<sup>1</sup>Downgraded 1 level due to study limitations (high risk of performance bias) and 1 level due to imprecision (small sample size of n = 59)

<sup>2</sup>Downgraded 1 level due to study limitations (high risk of performance bias) and 1 level due to imprecision (small sample size of n = 41)

<sup>3</sup>Downgraded 1 level due to study limitations (high risk of performance bias) and 1 level due to imprecision (small sample size of n = 59)

<sup>4</sup> Downgraded 1 level due to study limitations (high risk of performance bias) and 1 level due to imprecision (small sample size of n = 59)

Figure 1. Study flow diagram

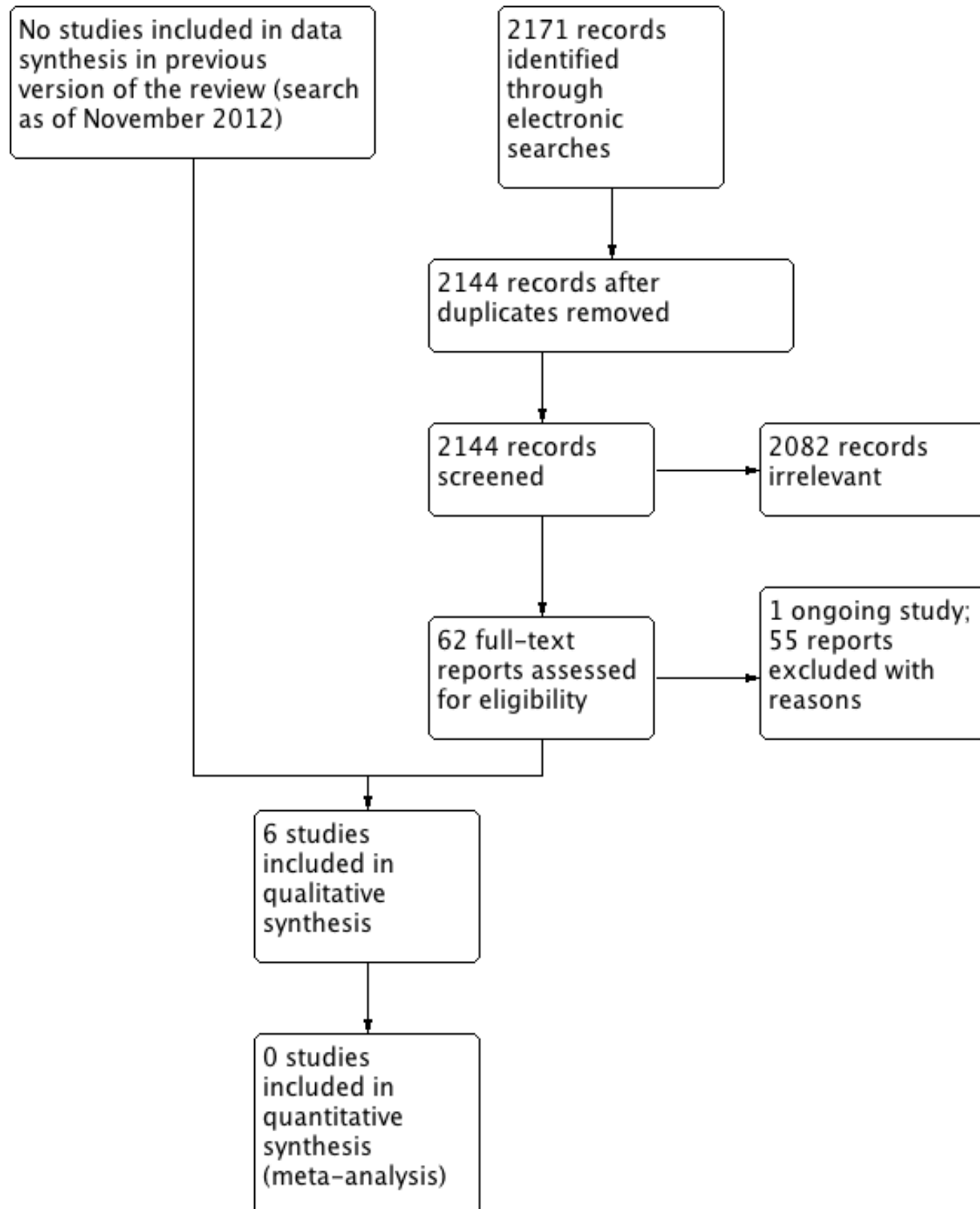


Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Adams 2018							
Campbell 2005							
Gleeson 2017							
Jeter 2015							
Kovacs 2012							
Waterman 2016							

Figure 3. Environmental intervention versus social/home visits comparison

1. Primary outcome of the review: Physical activity at 6 months				Estimate by group*			Effect estimate between groups	
	Outcome		Outcome (notes)	Intervention	Comparison	Estimate	95% CI	P value
1. Waterman 2016	Step counts	-		5321 (3892) 15	5000 (2192) 13	321	-1980.98, 2622.98	No statistically significant difference
	Walking time	-		70.2 (44.5) 15	68.5 (22.9) 13	1.7	-24.03, 27.43	No statistically significant difference
	Self-reporting physical activity - FITT	-		47.37 (18.84) 15	51.05 (25.72) 13	-3.68	-20.6, 13.24	No statistically significant difference
2. Primary outcome of the review: fall measures				Estimate by group*			Effect estimate between groups	
	Outcome		Outcome (notes)	Intervention	Comparison	Estimate	95% CI	P value
1. Waterman 2016	Proportion of fallers at 6 months	-		7/15	8/13	0.76	0.38, 1.51	No statistically significant difference
	Falls rate per person year at 6 months	-		2.32 (2.19) 15	1.58 (1.71) 13	0.74	-0.71, 2.19	No statistically significant difference
	Moderate injurious falls per person year at 6 months	-		0.86 (1.41) 15	0.24 (0.84) 13	0.61	-0.24, 1.46	No statistically significant difference
	Serious injurious falls per person year at 6 months	-		0.24 (0.83) 15	0 (0.41) 13	0.24	-0.24, 0.72	No statistically significant difference
2. Campbell 2005	Proportion of fallers at 12 months	-		36/100	59/96	0.59	0.43, 0.80	In favor of environmental intervention
	Proportion of injurious fallers at 12 months	-		39/100	65/96	0.58	0.43, 0.76	In favor of environmental intervention
	Falls rate per person year at 12 months	-		0.65	1.65	0.39	0.24, 0.62	In favor of environmental intervention
	Injurious falls rate per person year at 12 months	-		0.4	0.71	0.56	0.36, 0.87	In favor of environmental intervention
3. Secondary outcome of the review: fear of falling scores at 6 months				Estimate by group*			Effect estimate between groups	
	Outcome		Outcome (notes)	Intervention	Comparison	Estimate	95% CI	P value
1. Waterman 2016	Short Falls Efficacy Scale-International scores	-		12.93 (5.64) 15	10.38 (2.02) 13	2.55	-0.51, 5.61	No statistically significant difference
4. Secondary outcome of the review: quality of life at 6 months.				Estimate by group*			Effect estimate between groups	
	Outcome		Outcome (notes)	Intervention	Comparison	Estimate	95% CI	P value
1. Waterman 2016	SF-12 scores	-		42.89 (9.1) 15	46.03 (11.39) 13	-3.14	-10.86, 4.58	No statistically significant difference

\* Mean (standard deviation) sample size or Number of events/total  
CI: confidence interval

Figure 4. Behavioral intervention versus usual activity or social/home visits comparison

1. Primary outcome of the review: Physical activity at 6 months				Estimate by group*			Effect estimate between groups		
	Outcome		Outcome (notes)	Intervention	Comparison	Estimate	95% CI		P value
1. Adams 2018	Self-reporting physical activity - FITT at 3 months	-		55 (40.7) 29	47 (31.1) 31	8	-10.41, 26.41	No statistically significant difference	
	Self-reporting physical activity - FITT at 6 months	-		52.1 (51.9) 28	43 (35.6) 31	9.1	-13.85, 32.5	No statistically significant difference	
2. Primary outcome of the review: fall measures				Estimate by group*			Effect estimate between groups		
	Outcome		Outcome (notes)	Intervention	Comparison	Estimate	95% CI		P value
1. Kovacs 2012	Proportion of fallers at 6 months	-		8/21	14/20	0.54	0.29, 1.01	No statistically significant difference	
	Mean length of time to first fall in weeks	-		18.5 (7.36) 21	14.8 (8.32) 20	3.70	-1.12, 8.52	No statistically significant difference	
2. Campbell 2005	Proportion of fallers at 12 months	-		47/97	59/96	0.79	0.61, 1.02	No statistically significant difference	
	Proportion of injurious fallers at 12 months	-		53/97	65/96	0.89	0.70, 1.13	No statistically significant difference	
	Falls rate per person year at 12 months	-		1.3	1.65	0.79	0.48, 1.28	No statistically significant difference	
3. Gleeson 2015	Injurious falls rate per person year at 12 months	-		0.57	0.71	0.82	0.48, 1.40	No statistically significant difference	
	Proportion of fallers at 12 months	-		25/60	27/60	0.93	0.61, 1.39	No statistically significant difference	
	Proportion of injurious fallers at 12 months	-		27/60	37/60	0.73	0.52, 1.03	No statistically significant difference	
	Falls rate per person year at 12 months	-		1.01	1.49	0.67	0.36, 1.26	No statistically significant difference	
	Injurious falls rate per person year at 12 months	-		-	-	0.49	0.22, 1.11	No statistically significant difference	
3. Secondary outcome of the review: fear of falling scores				Estimate by group*			Effect estimate between groups		
	Outcome		Outcome (notes)	Intervention	Comparison	Estimate	95% CI		P value
1. Adams 2018	Short Falls Efficacy Scale-International scores at 3 months	-		9 (2.22) 29	8 (2.22) 30	1.00	-0.13, 2.13	No statistically significant difference	
	Short Falls Efficacy Scale-International scores at 6 months	-		8 (2.96) 28	8 (2.96) 31	0.00	-1.51, 1.51	No statistically significant difference	
2. Gleeson 2017	Short Falls Efficacy Scale-International scores at 3 months	-		12.08 (4.25) 55	12.96 (5.69) 59	-0.88	-2.72, 0.96	No statistically significant difference	
	Short Falls Efficacy Scale-International scores at 12 months	-		12.47 (4.18) 55	12.7 (5.65) 56	-0.23	-2.08, 1.62	No statistically significant difference	
3. Jeter 2015	Illinois fear of falling scores at 2 months	-	Method of aggregation not reported	-	-	-	-	No statistically significant difference	
4. Secondary outcome of the review: quality of life at 6 months.				Estimate by group*			Effect estimate between groups		
	Outcome		Outcome (notes)	Intervention	Comparison	Estimate	95% CI		P value
1. Adams 2018	European quality of life-15 scores at 3 months	-		-0.20 (0.22) 28	-0.12 (0.27) 31	-0.08	-0.21, 0.05	No statistically significant difference	
	European quality of life-15 scores at 6 months	-		-0.21 (0.27) 28	-0.06 (0.28) 31	-0.15	-0.29, -0.01	In favor of usual activity comparison	
2. Gleeson 2017	Geriatric Depression Scale (GDS-5) at 3 months	-		1.29 (1.39) 55	1.34 (1.47) 59	0.15	-0.36, 0.66	No statistically significant difference	
	Geriatric Depression Scale (GDS-5) at 12 months	-		1.13 (1.16) 55	1.14 (1.37) 56	-0.01	-0.48, 0.46	No statistically significant difference	
	Positive and Negative Affect Scale (PANAS) at 3 months	-		36.04 (6.69) 55	34.57 (7.56) 59	1.47	-1.15, 4.09	No statistically significant difference	
	Positive and Negative Affect Scale (PANAS) at 12 months	-		35.04 (8.55) 55	35.82 (7.21) 56	-0.78	-3.72, 2.16	No statistically significant difference	

\* Mean (standard deviation) sample size or Number of events/total  
CI: confidence interval

Figure 5. Environmental intervention versus behavioral comparison

1. Primary outcome of the review: fall measures				Estimate by group*		Effect estimate between groups		
	Outcome	Outcome (notes)		Intervention	Comparison	Estimate	95% CI	P value
1. Campbell 2005	Proportion of fallers at 12 months	-		36/100	47/97	0.74	0.53, 1.02	No statistically significant difference
	Proportion of injurious fallers at 12 months	-		39/100	53/97	0.66	0.48, 0.91	In favor of environmental intervention

\* Mean (standard deviation) sample size or Number of events/total  
CI: confidence interval



Figure 6. Environmental and behavioral intervention versus social/home visits comparison

1. Primary outcome of the review: Physical activity at 6 months				Estimate by group*			Effect estimate between groups	
	Outcome	Outcome (notes)		Intervention	Comparison	Estimate	95% CI	P value
1. Waterman 2016	Step counts	-		3927 (1815) 15	5000 (2192) 13	-1073	-2577.48, 431.48	No statistically significant difference
	Walking time	-		55 (24.8) 15	68.5 (22.9) 13	-13.15	-31.18, 4.18	No statistically significant difference
	Self-reporting physical activity - FITT	-		42.56 (13.62) 15	47.92 (14.92) 13	-5.36	-16.01, 5.29	No statistically significant difference
2. Primary outcome of the review: fall measures				Estimate by group*			Effect estimate between groups	
	Outcome	Outcome (notes)		Intervention	Comparison	Estimate	95% CI	P value
1. Waterman 2016	Proportion of fallers at 6 months	-		9/15	8/13	0.97	0.54, 1.77	No statistically significant difference
	Falls rate per person year at 6 months	-		2.22 (2.16) 15	1.58 (1.71) 13	0.64	-0.80, 2.08	No statistically significant difference
	Moderate injurious falls per person year at 6 months	-		0.37 (0.99) 15	0.24 (0.84) 13	0.13	-0.55, 0.81	No statistically significant difference
	Serious injurious falls per person year at 6 months	-		0 (0.44) 15	0 (0.41) 13	0.00	-0.32, 0.32	No statistically significant difference
2. Campbell 2005	Proportion of fallers at 12 months	-		47/98	59/96	0.78	0.60, 1.01	No statistically significant difference
	Proportion of injurious fallers at 12 months	-		61/98	65/96	1.01	0.81, 1.26	No statistically significant difference
	Falls rate per person year at 12 months	-		1.17	1.65	-	-	-
	Injurious falls rate per person year at 12 months	-		0.66	0.71	-	-	-
3. Secondary outcome of the review: fear of falling scores at 6 months				Estimate by group*			Effect estimate between groups	
	Outcome	Outcome (notes)		Intervention	Comparison	Estimate	95% CI	P value
1. Waterman 2016	Short Falls Efficacy Scale-International scores	-		11.5 (4.7) 15	10.38 (2.02) 13	1.12	-1.50, 3.74	No statistically significant difference
4. Secondary outcome of the review: quality of life at 6 months.				Estimate by group*			Effect estimate between groups	
	Outcome	Outcome (notes)		Intervention	Comparison	Estimate	95% CI	P value
1. Waterman 2016	SF-12 scores	-		43.21 (8.61) 15	46.03 (11.39) 13	-2.82	-10.39, 4.75	No statistically significant difference

\* Mean (standard deviation) sample size or Number of events/total  
CI: confidence interval

Figure 7. Environmental and behavioral intervention versus environmental comparison

1. Primary outcome of the review: Physical activity at 6 months				Estimate by group*			Effect estimate between groups	
	Outcome	Outcome (notes)		Intervention	Comparison	Estimate	95% CI	P value
1. Waterman 2016	Step counts	-		3927 (1815) 15	5321 (3892) 15	-1394	-3567.23, 779.23	No statistically significant difference
	Walking time	-		55 (24.8) 15	70.2 (44.5) 15	-15.2	-40.98, 10.58	No statistically significant difference
	Self-reporting physical activity - FITT	-		51.97 (22.27) 15	47.37 (18.64) 15	4.6	-10.10, 19.30	No statistically significant difference
2. Primary outcome of the review: fall measures				Estimate by group*			Effect estimate between groups	
	Outcome	Outcome (notes)		Intervention	Comparison	Estimate	95% CI	P value
1. Waterman 2016	Proportion of fallers at 6 months	-		9/15	7/15	0.78	0.39, 1.54	No statistically significant difference
	Falls rate per person year at 6 months	-		2.22 (2.16) 15	2.32 (2.19) 15	-0.1	-1.66, 1.46	No statistically significant difference
	Moderate injurious falls per person year at 6 months	-		0.37 (0.99) 15	0.85 (1.41) 15	-0.48	-1.35, 0.39	No statistically significant difference
	Serious injurious falls per person year at 6 months	-		0 (0.44) 15	0.24 (0.83) 15	-0.24	-0.72, 0.24	No statistically significant difference
2. Campbell 2005	Proportion of fallers at 12 months	-		47/98	36/100	1.33	0.95, 1.85	No statistically significant difference
	Proportion of injurious fallers at 12 months	-		61/98	39/100	1.56	1.17, 2.09	In favor of environmental comparison
	Falls rate per person year at 12 months	-		1.17	0.65	-	-	-
	Injurious falls rate per person year at 12 months	-		0.66	0.40	-	-	-
3. Secondary outcome of the review: fear of falling scores at 6 months				Estimate by group*			Effect estimate between groups	
	Outcome	Outcome (notes)		Intervention	Comparison	Estimate	95% CI	P value
1. Waterman 2016	Short Falls Efficacy Scale-International scores	-		11.5 (4.7) 15	12.93 (5.64) 15	-1.43	-5.15, 2.29	No statistically significant difference
4. Secondary outcome of the review: quality of life at 6 months.				Estimate by group*			Effect estimate between groups	
	Outcome	Outcome (notes)		Intervention	Comparison	Estimate	95% CI	P value
1. Waterman 2016	SF-12 scores	-		43.21 (8.61) 15	42.89 (9.10) 15	0.32	-6.02, 6.66	No statistically significant difference

\* Mean (standard deviation) sample size or Number of events/total  
CI: confidence interval

Figure 8. Environmental and behavioral intervention versus behavioral comparison

1. Primary outcome of the review: fall measures			Estimate by group*			Effect estimate between groups		
	Outcome	Outcome (notes)	Intervention	Comparison	Estimate	95% CI	P value	
1. Campbell 2005	Proportion of fallers at 12 months	-	47/98	47/97	0.99	0.74, 1.32	No statistically significant difference	
	Proportion of injurious fallers at 12 months	-	61/98	53/97	1.14	0.90, 1.45	No statistically significant difference	
	Falls rate per person year at 12 months	-	1.17	1.30	-	-		
	Injurious falls rate per person year at 12 months	-	0.66	0.57	-	-		

\* Mean (standard deviation) sample size or Number of events/total  
CI: confidence interval

## Appendices

### *1 CENTRAL search strategy*

- #1 MeSH descriptor Vision Disorders
- #2 MeSH descriptor Visually Impaired Persons
- #3 (low\* or handicap\* or subnormal\* or impair\* or partial\* or disab\*) near/3 (vision or visual\* or sight\*)
- #4 (#1 OR #2 OR #3)
- #5 MeSH descriptor Rehabilitation
- #6 (rehabilitat\* or assess\*) near/4 (low vision)
- #7 MeSH descriptor Activities of Daily Living
- #8 MeSH descriptor Risk Assessment
- #9 MeSH descriptor Risk Factors
- #10 MeSH descriptor Risk Management
- #11 MeSH descriptor Safety Management
- #12 (home near/3 safet\*)
- #13 (hazard\*) near/3 (home or environment\*)
- #14 MeSH descriptor Home Care Services
- #15 MeSH descriptor Occupational Therapy
- #16 MeSH descriptor Exercise Therapy
- #17 MeSH descriptor Physical Therapy Modalities
- #18 behavio\* near/3 modif\*
- #19 (program\*) near/3 (home or exercise\* or modif\*)
- #20 MeSH descriptor Cognitive Therapy
- #21 MeSH descriptor Behavior Therapy
- #22 (#5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21)
- #23 (#4 AND #22)

### *2 MEDLINE (OvidSP) search strategy*

- 1. randomized controlled trial.pt.
- 2. (randomized or randomised).ab,ti.
- 3. placebo.ab,ti.
- 4. dt.fs.
- 5. randomly.ab,ti.
- 6. trial.ab,ti.
- 7. groups.ab,ti.
- 8. or/1-7
- 9. exp animals/
- 10. exp humans/
- 11. 9 not (9 and 10)
- 12. 8 not 11
- 13. exp vision disorders/

14. exp visually impaired persons/
15. ((low\$ or handicap\$ or subnormal\$ or impair\$ or partial\$ or disab\$) adj3 (vision or visual\$ or sight\$)).tw.
16. or/13-15
17. exp rehabilitation/
18. ((rehabilitat\$ or assess\$) adj4 low vision).tw.
19. exp activities of daily living/
20. risk assessment/
21. risk factors/
22. risk management/
23. safety management/
24. (home adj3 safety\$).tw.
25. (hazard\$ adj3 (home or environment\$)).tw.
26. home care services/
27. occupational therapy/
28. exercise therapy/
29. physical therapy modalities/
30. (behavio\$ adj3 modif\$).tw.
31. (program\$ adj3 (home or exercise\$ or modif\$)).tw.
32. Cognitive Therapy/
33. Behavior Therapy/
34. or/17-33
35. 16 and 34
36. 12 and 35

The search filter for trials at the beginning of the MEDLINE strategy is from the published paper by Glanville et al ([Glanville 2006](#)).

### *3 EMBASE (OvidSP) search strategy*

1. exp randomized controlled trial/
2. exp randomization/
3. exp double blind procedure/
4. exp single blind procedure/
5. random\$.tw.
6. or/1-5
7. (animal or animal experiment).sh.
8. human.sh.
9. 7 and 8
10. 7 not 9
11. 6 not 10
12. exp clinical trial/
13. (clin\$ adj3 trial\$).tw.
14. ((singl\$ or doubl\$ or trebl\$ or tripl\$) adj3 (blind\$ or mask\$)).tw.
15. exp placebo/

16. placebo\$.tw.
17. random\$.tw.
18. exp experimental design/
19. exp crossover procedure/
20. exp control group/
21. exp latin square design/
22. or/12-21
23. 22 not 10
24. 23 not 11
25. exp comparative study/
26. exp evaluation/
27. exp prospective study/
28. (control\$ or prospectiv\$ or volunteer\$).tw.
29. or/25-28
30. 29 not 10
31. 30 not (11 or 23)
32. 11 or 24 or 31
33. exp vision disorder/
34. exp visual impairment/
35. ((low\$ or handicap\$ or subnormal\$ or impair\$ or partial\$ or disab\$) adj3 (vision or visual\$ or sight\$)).tw.
36. or/33-35
37. exp rehabilitation/
38. ((rehabilitat\$ or assess\$) adj4 low vision).tw.
39. exp daily life activities/
40. risk assessment/
41. risk factor/
42. exp home safety/
43. (home adj3 safety\$).tw.
44. exp falling/
45. (hazard\$ adj3 (home or environment\$)).tw.
46. home care/
47. occupational therapy/
48. kinesiotherapy/
49. exp physiotherapy/
50. (behavio\$ adj3 modif\$).tw.
51. (program\$ adj3 (home or exercise\$ or modif\$)).tw.
52. Cognitive Therapy/
53. Behavior Therapy/
54. or/37-53
55. 36 and 54
56. 32 and 55

#### *4 CINAHL (EBSCO) search strategy*

S42 S40 and S41  
 S41 (MH "Aged+") OR (MH "Aged, 80 and Over") OR (MH "Frail Elderly")  
 S40 S12 and S39  
 S39 S20 and S38  
 S38 S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29 or S30 or S31 or S32 or S33  
 or S34 or S35 or S36 or S37  
 S37 (MH "Behavior Therapy+") OR (MH "Behavior Therapy (Iowa NIC) (Non-Cinahl)")  
 S36 (MH "Cognitive Therapy") OR (MH "Cognitive Therapy (Iowa NIC) (Non-Cinahl)")  
 S35 TX ((program\* n3 home) or (program\* n3 exercise) or (program\* n3 modif\*))  
 S34 TX behavio\* n3 modif\*  
 S33 (MH "Physical Therapy")  
 S32 (MH "Exercise Therapy: Ambulation (Iowa NIC)") OR (MH "Exercise Therapy: Balance  
 (Iowa NIC)")  
 S31 (MH "Occupational Therapy+")  
 S30 (MH "Home Health Care")  
 S29 TX ((hazard\* n3 home) or (hazard\* n3 environment\*))  
 S28 TX home n3 safety\*  
 S27 (MH "Risk Management") OR (MH "Risk Management (Iowa NIC) (Non-Cinahl)")  
 S26 (MH "Risk Factors")  
 S25 (MH "Risk Assessment") OR (MH "Fall Risk Assessment Tool")  
 S24 (MH "Activities of Daily Living+") OR (MH "Activities of Daily Living (Saba CCC)") OR  
 (MH "Activities of Daily Living Alteration (Saba CCC)") OR (MH "Instrumental Activities of  
 Daily Living (Saba CCC)") OR (MH "Instrumental Activities of Daily Living Alteration (Saba  
 CCC)") OR (MH "Altered Activities of Daily Living (NANDA) (Non-Cinahl)") OR (MH "Self  
 Care: Activities of Daily Living (Iowa NOC)") OR (MH "Self-Care: Instrumental Activities of  
 Daily Living (Iowa NOC)")  
 S23 TX assess\* n4 vision\*  
 S22 TX rehabilitat\* n4 vision\*  
 S21 (MH "Rehabilitation of Vision Impaired+")  
 S20 S13 or S14 or S15 or S16 or S17 or S18 or S19  
 S19 TX ((disab\* n3 vision) or (disab\* n3 visual\*) or (disab\* n3 sight))  
 S18 TX ((partial\* n3 vision) or (partial\* n3 visual\*) or (partial\* n3 sight))  
 S17 TX ((impair\* n3 vision) or (impair\* n3 visual\*) or (impair\* n3 sight))  
 S16 TX ((subnormal\* n3 vision) or (subnormal\* n3 visual\*) or (subnormal\* n3 sight))  
 S15 TX ((handicap\* n3 vision) or (handicap\* n3 visual\*) or (handicap\* n3 sight))  
 S14 TX ((low\* n3 vision) or (low\* n3 visual\*) or (low\* n3 sight))  
 S13 (MH "Vision Disorders+")  
 S12 S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10 or S11  
 S11 TX allocat\* random\*  
 S10 (MM "Quantitative Studies")  
 S9 (MM "Placebos")  
 S8 TX placebo\*  
 S7 TX random\* allocat\*  
 S6 (MM "Random Assignment")  
 S5 TX randomi\* control\* trial\*  
 S4 TX ( (singl\* n1 blind\*) or (singl\* n1 mask\*) ) or TX ( (doubl\* n1 blind\*) or (doubl\* n1

mask\*) ) or TX ( (tripl\* n1 blind\*) or (tripl\* n1 mask\*) ) or TX ( (trebl\* n1 blind\*) or (trebl\* n1 mask\*) )

S3 TX clinic\* n1 trial\*

S2 PT Clinical trial

S1 (MH "Clinical Trials+")

#### *5 AMED (OvidSP) search strategy*

1. vision disorders/
2. ((low\$ or handicap\$ or subnormal\$ or impair\$ or partial\$ or disab\$) adj3 (vision or visual\$ or sight\$)).tw.
3. or/1-2
4. Rehabilitation/
5. ((rehabilitat\$ or assess\$) adj4 low vision).tw.
6. "Activities of daily living"/
7. Risk/
8. Safety/
9. (home adj3 safety\$).tw.
10. (hazard\$ adj3 (home or environment\$)).tw.
11. Home care services/
12. Occupational therapy/
13. Exercise therapy/
14. physical therapy modalities/
15. (behavio\$ adj3 modif\$).tw.
16. (program\$ adj3 (home or exercise\$ or modif\$)).tw.
17. Cognitive therapy/
18. Behavior therapy/
19. or/4-18
20. 3 and 19
21. "Randomized controlled trials"/
22. prospective studies/
23. single blind method/
24. random\$.tw.
25. placebo\$.tw.
26. trial\$.tw.
27. groups.tw.
28. ((singl\$ or doubl\$) adj3 (blind\$ or mask\$)).tw.
29. or/21-28
30. 20 and 29

#### *6 OTseeker search strategy*

low vision AND rehabilitation AND random



*7 metaRegister of Controlled Trials search strategy*

low vision and rehabilitation

*8 ClinicalTrials.gov search strategy*

Low Vision AND Rehabilitation

*9 ICTRP search strategy*

Low Vision AND Rehabilitation

*10 List of abbreviations*

Phone-FITT: Telephone questionnaire for self-report of physical activity

SFES-I: Short Falls Efficacy Scale-International

EuroQoL: European Quality of Life

GDS: Geriatric Depression Scale

PANAS: Positive and Negative Affect Scale

O&M: Orientation and Mobility

PASE: Physical Activity Scale for the Elderly

SF-12: 12-Item Short Form Health Survey

SD-36: 36-Item Short Form Health Survey

AFRIS: Attitudes to Falls-Related Interventions Scale

FABQ: Fear-Avoidance Beliefs Questionnaire

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## Chapter 3

### Characterizing the Impact of Fear of Falling on Activity and Falls in Older Adults with Glaucoma

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Keywords: falls; fear of falling; glaucoma; older adults; physical activity; vision loss

Manuscript word count: 3160

## Abstract

**Objective:** Fear of falling (FoF) may alter mobility in older adults, especially among those with visual impairment. Using a longitudinal prospective cohort of older glaucoma patients, we investigated whether and how FoF is associated with future falls and physical activity.

**Design:** Prospective, observational cohort study.

**Setting:** Hospital-based, single center recruitment.

**Participants:** Individuals with glaucoma or suspected glaucoma.

**Measurements:** FoF was measured annually over a 3-year period using the University of Illinois at Chicago FoF Questionnaire, with lower Rasch-analyzed FoF scores (in logit units) indicating less fear. Participants recorded falls prospectively over the 3-year period using monthly mail-in calendars. Daily steps were collected annually over 7-days using an accelerometer. Visual field (VF) sensitivity was derived by combining sensitivities from monocular VF results. Participants completed questionnaires to determine other demographic/health characteristics. Multivariate random-effects models evaluated within-participant changes in fall rates and physical activity across study years.

**Results:** At lower FoF levels ( $\text{FoF} \leq 0$ ), each one-unit worsening in FoF score across study years was associated with 2.73 times higher odds of reporting at least one fall in the next year (95% CI: 1.55, 4.81) but was not associated with average daily steps ( $p=0.44$ ). Similar results were seen when fall rates were normalized by number of steps taken ( $p=0.97$ ). At higher FoF levels ( $\text{FoF} > 0$ ), inter-year changes in FoF scores were not significantly associated with reporting a fall in the next year ( $p=0.78$ ); but were associated with 407 fewer average daily steps per one-unit change in FoF (95% CI: -743, -71).

Conclusion: FoF is an important psychological factor that is associated with mobility in glaucoma patients, though specific aspects of mobility (fall rates vs. activity levels) affected vary by the degree of FoF. Our findings suggest that customizing behavioral interventions for older adults based on their levels of FoF may be an important strategy for fall prevention and activity promotion.

## Introduction

Fear of Falling (FoF) is a common long-lasting psychological consequence of falling in older adults.<sup>1</sup> Individuals with greater FoF more often avoid physical activity,<sup>2</sup> travel less outside the home,<sup>3</sup> reduce social interactions,<sup>4</sup> and transition to assisted living than individuals with less FoF.<sup>5</sup> Together, these FoF consequences may impact quality of life.

FoF is a prevalent concern among people with vision loss, particularly those with visual field (VF) damage.<sup>6,7</sup> In evaluating fall prevention programs, FoF is frequently used as an outcome, given the strong associations between FoF and mobility outcomes, and the time and effort required to prospectively ascertain falls.<sup>8,9</sup> This use of FoF as an outcome in these programs presumes that FoF serves as a fall risk factor which is often evaluated as a proximal outcome for other events that are hard to measure,<sup>10</sup> i.e., fall rates and/or physical activity, though such associations are not well established in the literature.

Previous studies have noted cross-sectional associations between FoF and physical activity.<sup>11-13</sup> However, few studies have measured FoF, physical activity, and fall rates longitudinally to link changes in FoF to changes in physical activity or fall rates. A better understanding of the associations among FoF, physical activity, and falls will clarify whether FoF is an appropriate proximal measure in interventions aimed at preserving physical activity and preventing falls.

The objective of this study was to examine the longitudinal association of FoF with future falls and physical activity in persons with glaucoma. We hypothesized that, within an individual, time

points with greater FoF would demonstrate higher fall rates and lower accelerometer-defined physical activity.

## **Methods**

### *Participants*

Study participants were recruited into the Falls in Glaucoma Study (FIGS), a single-center prospective study conducted at Johns Hopkins Wilmer Eye Institute from 2013-2015.

Participants were eligible if they were aged  $\geq 60$ , lived within 60 miles of Baltimore, diagnosed with primary/suspected glaucoma, and able to perform VF testing. Detailed inclusion and exclusion criteria are described elsewhere.<sup>14</sup>

We compared the characteristics of recruited study participants to a study-eligible population from the same clinic over a one-week period (258 patients); recruited participants had a higher risk of falling and likelihood of using assistive devices than the overall patient population from which they were recruited.

### *Measures*

We assessed FoF using the University of Illinois at Chicago FoF Questionnaire.<sup>15</sup> The questionnaire was administered annually at baseline and follow-up visits. Participants rated their FoF as “very worried”, “moderate/a little worried” or “not worried” for 18 different tasks ranging from easy activities (e.g., getting out of a car), to hard activities (e.g., walking on icy ground). Rasch modeling matched personal ability (i.e., person measure scores) to task difficulty

(i.e., item measure scores) on the same linear scale in log-odds (logit) units using MPlus.<sup>16</sup> FoF was taken as the inverse of Rasch-derived person-measure scores, such that higher scores reflected greater FoF, while lower scores reflected less FoF. We anchored FoF scores in follow-up visits to first year FoF score for each individual such that all FoF scores were obtained from the same Rasch model.

Falls were described to participants as “unintentionally coming to rest on the ground or at some other level,” and illustrated using an instructional video.<sup>6,17</sup> Participants were asked to mark falls calendars daily to indicate the presence or absence of a fall and to return calendar data at the end of the month via mail or email.

Physical activity was measured using a waist-bound omnidirectional accelerometer (Actical, Respironics Inc., Murrysville, PA) for a one-week period occurring at the start of each study year. We used data from these one-week accelerometer trials to project average daily steps over the upcoming year.<sup>18</sup> As previously described, a minimum of four valid days of accelerometer data were required for inclusion in the analysis.<sup>18</sup>

We evaluated fall rates as falls per unit time (year) and falls per unit activity (step), as fall rates might be diminished in persons restricting their physical activity.

Baseline vision tests included visual acuity (using the ETDRS chart) and VF testing on a Humphrey HFA-2 perimeter. We derived integrated VF (IVF) sensitivity by combining pointwise sensitivities from both eyes to generate a sensitivity at each spatial coordinate using the



maximum sensitivity approach.<sup>14</sup> The average IVF for normal VFs was  $\geq 31$  decibels (dB), with lower values suggesting VF damage. The degree of VF damage was categorized as: normal/mild (IVF  $> 28$  dB), moderate (IVF 23-28 dB), and severe (IVF  $< 23$  dB).<sup>19</sup>

Baseline demographic characteristics were obtained via questionnaire. We defined polypharmacy as  $\geq 5$  non-eyedrops by directly observing medication containers or asking about medications used via questionnaire. We assessed cognitive ability using Mini-Mental State Exam for visually impaired (MMSE-VI), which classified dementia as a score  $\leq 16$  and no dementia as 17-22.<sup>20</sup> We summed the number of comorbidities from the list of comorbid conditions reported previously.<sup>21</sup>

### *Statistical Analysis*

We used Generalized Estimation Equation (GEE) model for testing with correlated longitudinal data (including all three years) and chose the appropriate correlation structure by comparing how accurately the unstructured, autocorrelation and exchangeable structure models predicted the true relationship between FoF and outcomes. To estimate the subject-specific association, we used (i) logistic random-effects regression models to examine the association between FoF and subsequent falls in the next year; (ii) linear random-effects regression models to test the association between FoF and average daily steps; and (iii) random-effects negative binomial regression models to assess whether FoF was associated with subsequent falls measured by falls/year and falls/step.

## **Results**

The 243 study participants had a median age of 70 years (IQR: 64-75), and 28.8% (70) were African American, 48.6% (118) were female, 20.2% (49) lived alone, and 84.8% (206) had some college education or more (Table 1). Additionally, 65.0% (158) had  $\geq 2$  comorbidities, 45.3% (111) used  $\geq 5$  prescription medications, and mean MMSE-VI score was 20 (standard deviation [SD]=1.6). Median IVF sensitivity was 27.0 dB (IQR: 26.1-30.0). Roughly half (49.4%) of participants had mild/normal VF damage, while 40.3% and 10.3% had moderate and severe VF damage, respectively. Median visual acuity-logMAR was 0.1 (IQR: 0-0.2), with a median Snellen equivalent of 20/23.

FoF was measured in 243 participants in the first year (mean=0.04, SD=0.90), 228 (93.8%) in the 2<sup>nd</sup> year (mean=0.06, SD=0.93) and 207 (85.2%) in the 3<sup>rd</sup> year (mean=0.07, SD=0.92). Over the three-year study period, 44.9%, 36.0% and 24.6% of participants experienced at least one fall in the first year, 2<sup>nd</sup> and 3<sup>rd</sup> year, respectively.

The likelihood of falling in the upcoming year (Figure 1A) and accelerometry defined physical activity (Figure 1B) varied with the level of fear of falling, with exchangeable structure model chosen to predict the true relationships between FoF and reporting at least one fall in the next year (Figure 1A) and average daily steps (Figure 1B) based on the quality of fit. At lower FoF levels (FoF $\leq 0$ ), each one-unit worsening in FoF score across study years was associated with a 2.73 times higher odds of reporting at least one fall in the next year (95% CI: 1.55, 4.81); there was no evidence of association of FoF score with changes in average daily steps ( $p=0.44$ ) (Table 2). At higher FoF levels (FoF $>0$ ), each one-unit worsening in FoF across study years was not

associated with reporting at least one fall in the next year ( $p=0.78$ ), but was associated with 407 fewer average daily steps (95% CI: -743, -71).

Additional analyses assessed the impact of FoF on fall rates, which also varied across level of FoF, and was well-modeled using the exchangeable structure (Figure 1C). At lower FoF levels ( $\text{FoF} \leq 0$ ), each one-unit worsening in FoF score across study years was associated with a 2.20 fold higher rates of falls/year (95% CI: 1.47, 3.29) (Table 2). At higher FoF levels ( $\text{FoF} > 0$ ), there was no evidence of associations between changes in FoF and either falls/year ( $p=0.41$ ) or falls/step ( $p=0.94$ ).

## **Discussion**

We characterized within-subject changes in fall rates and physical activity associated with changes in FoF in older adults with varying degrees of visual impairment, including some with normal VFs. The implications of FoF on mobility (falls and physical activity) depended on the level of FoF. At lower FoF levels, increases in FoF were associated with a higher risk of falls, but not activity decline. At higher levels of FoF, increases in FoF did not increase the risk of falls, but were associated with declines in physical activity. These findings suggest that physical activity declines may result only after FoF reaches a certain threshold, and that the consequences of FoF are not uniform.

Our results add to the literature suggesting higher FoF levels are associated with a greater future fall risk.<sup>22,23</sup> However, cross-sectional designs in prior studies prevented them from

characterizing how within-individual fall rates change over time as FoF rises/falls. Although cohort studies have suggested that baseline FoF level was an independent predictor for falls,<sup>24</sup> these studies often measured falls by asking questions prone to recall bias, i.e. “have you fallen last year”.<sup>25</sup> As such, authors comparing retrospective and prospective falls data collection methods have recommended prospective evaluation of falls using tools such as calendars to improve the accuracy.<sup>26</sup> Additionally, prior studies often dichotomized FoF through a single question, e.g., “do you ever limit activities because you are afraid of falling”.<sup>24</sup> This question has limited sensitivity to evaluate whether fall consequences are constant across levels of FoF. Our findings suggest that greater FoF, measured via a reliable and valid questionnaire, predict future fall risk in older adults, but only at lower FoF levels.

Our study also investigated whether changes in FoF were associated with changes in physical activity. Previous research often measured physical activity using questionnaires, which are poorly correlated with objectively-measured physical activity.<sup>27,28</sup> One study did find that FoF has a negative and significant association on objectively-measured physical activity,<sup>29</sup> with persons with high FoF demonstrating less physical activity. These findings do not necessarily, however, imply that longitudinal changes in FoF are likely to associated with changes in physical activity. In our study, we demonstrated that reductions in physical activity occur with worsening in FoF, but only at higher FoF levels.

Based on the findings from our study, the use of FoF as a risk factor that associated with mobility is justifiable, as changes in FoF are associated with changes in fall rates and physical activity for that individual. Our study did not investigate the mechanisms behind changes in FoF,

and it is possible that the mobility implications resulting from intervention-produced changes in FoF (e.g., rehabilitative or environmental approaches) may differ from those occurring naturally over time. Our findings do suggest that when individuals have low FoF levels, they may not perceive themselves as particularly at risk for fall-related injuries, such that changes within this range of FoF result in more falls, but not behavioral changes (i.e., less activity) to avoid falls. At higher FoF levels, individuals decreased activity as FoF worsened, while not experiencing a higher risk of falls, suggesting that they may have been more aware of the potential risk for fall-related injuries, and restricted their activity to avoid additional falls.

This study has limitations. First, our findings may not be generalizable to all older adults with vision loss because participants were recruited from a single center with one condition (i.e., glaucoma). Second, it is not clear whether FoF changes occurring in the context of other diseases (i.e. non-visual disorders) will affect fall rates and physical activity in the same way. Third, although we obtained FoF scores during annual assessment, the time interval was wide and FoF may have changed over the course of the year. However, our results are substantially powerful by characterizing within-subject changes in mobility as the confounders within an individual are less likely to change over a short period.

In summary, our findings validate the importance of FoF on mobility, and highlight that the implication of FoF changes on these measures is complex – affecting both physical activity and fall rates, but with different effects depending on the level of FoF. Further studies are warranted to examine whether interventions that target FoF will have an impact on future falls or activity changes.

## **Acknowledgement**

The research was supported in part by National Institutes of Health Grant EY022976.

## **Conflict of Interest**

Authors have no conflict of interest to declare.

## **CRedit authorship contribution statement**

**Jian-Yu E:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Validation, Visualization, Writing - original draft, Writing - review & editing.

**Aleksandra Mihailovic:** Conceptualization, Data curation, Project administration, Methodology, Validation, Writing - review & editing. **Pei-Lun Kup:** Data curation, Methodology, Writing - review & editing. **Sheila K. West:** Funding acquisition, Methodology, Validation, Writing - review & editing. **David S. Friedman:** Funding acquisition, Methodology, Validation, Writing - review & editing. **Laura N. Gitlin:** Funding acquisition, Methodology, Validation, Writing - review & editing. **Tianjing Li:** Conceptualization, Methodology, Supervision, Writing - review & editing. **Jennifer Schrack:** Conceptualization, Methodology, Supervision, Writing - review & editing. **Pradeep Y. Ramulu:** Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing - review & editing.

## **Sponsor's Role:**

The founding organization play no role in the design and conduct of this research.

Table 1. Characteristics of participants in Falls in Glaucoma Study at baseline.

	Values (N = 243)
<b>Demographics</b>	
Age, median (IQR)	70 (64.0-75.0)
African American, n (%)	70 (28.8%)
Female, n (%)	118 (48.6%)
Living alone, n (%)	49 (20.2%)
Education, n (%)	
≤ High school	37 (15.2%)
Some college	33 (13.6%)
Bachelor's degree	59 (24.3%)
Master's degree or higher	114 (46.9%)
<b>Health</b>	
No. of comorbid illnesses	
≤ 1, n (%)	85 (35.0%)
2-3, n (%)	107 (44.0%)
4-5, n (%)	51 (21.0%)
Polypharmacy, n (%)	111 (45.3%)
Overall MMSE-VI score, max as 22, mean (SD)	20 (1.6)
<b>Vision</b>	
IVF (dB), median (IQR)	27 (26.1-30.0)
Normal/mild visual field damage (IVF: >28 dB), n (%)	120 (49.4)
Moderate visual field damage (IVF: 23-28 dB), n (%)	98 (40.3)
Severe visual field damage (IVF: <23 dB), n (%)	25 (10.3)
Better-eye visual acuity-logMAR, median (IQR)	0.1 (0-0.2)
Snellen equivalent of visual acuity-logMAR, median (IQR)	20/23 (20/19-20/27)

IQR: interquartile range; SD: standard deviation; Polypharmacy: ≥5 systemic prescription medications; MMSE-VI: Mini-Mental State Examination-Visually Impaired; IVF: Integrated Visual Field; dB: decibels logMAR: logarithm of the minimum angle of resolution

Table 2: Within-individual changes in falls and activity outcomes with changes in fear of falling, stratified by level of fear of falling.

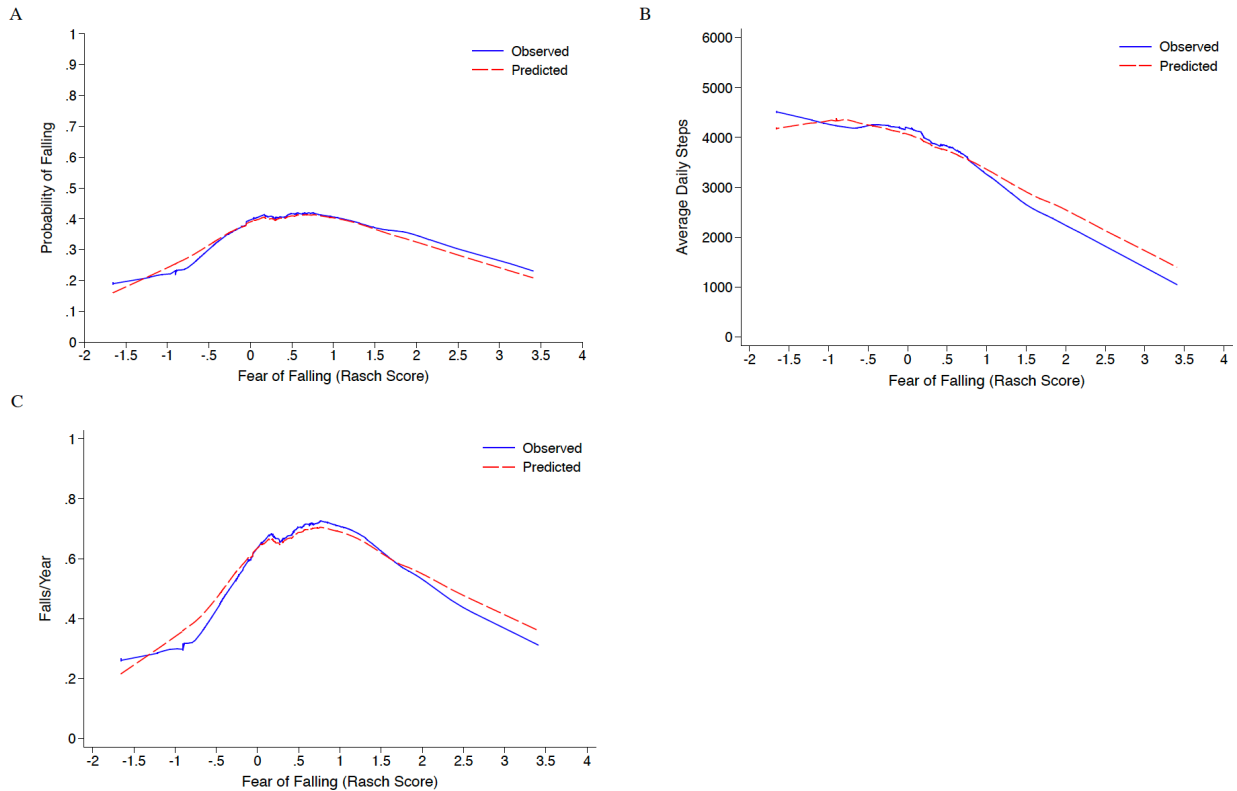
Outcome measured	FoF Rasch score	Unadjusted	P-value	Adjusted*	P-value
<b>Probability of falling</b>		<b>Odds ratios</b>			
	≤ 0	2.91 (1.63, 5.20)	<0.01	2.73 (1.55, 4.81)	<0.01
	> 0	0.83 (0.56, 1.24)	0.36	0.78 (0.52, 1.17)	0.23
<b>Avg daily steps</b>		<b>Difference in avg daily steps</b>			
	≤ 0	9.76 (-465.72, 482.24)	0.97	180.77 (-280.17, 641.70)	0.44
	> 0	-612.88 (-959.72, 266.05)	<0.01	-407.17 (-743.09, -71.25)	0.02
<b>Falls/year</b>		<b>Rate ratios</b>			
	≤ 0	2.26 (1.52, 3.37)	0.01	2.20 (1.47, 3.29)	0.01
	> 0	0.89 (0.68, 1.17)	0.41	0.89 (0.67, 1.17)	0.41
<b>Falls/step</b>		<b>Rate ratios</b>			
	≤ 0	2.71 (1.33, 3.38)	0.90	1.89 (1.03, 2.25)	0.94
	> 0	1.31 (0.39, 1.32)	0.94	1.21 (0.36, 2.11)	0.97

\*Adjusted for age, race, gender, living arrangement, education, comorbidity, polypharmacy, cognitive function, and visual field sensitivity.

FoF: fear of falling; Avg: average.



Figure 1. Observed versus predicted relationship between fear of falling and mobility measures (falls and physical activity).



(A) Relationship of fear of falling to the probability of a calendar record at least one fall in the following year. (B) Relationship of fear of falling to accelerometry-defined daily steps. (C) Relationship of fear of falling to the rate of falls/year. Note. An exchangeable correlation structure is used in predicted model. Higher fear of falling scores reflect greater fear of falling, while lower scores reflect less fear of falling.

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# Chapter 4

## Patterns of Daily Physical Activity Across the Spectrum of Visual Field Damage in Glaucoma Patients

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**Keywords:** activity fragmentation, activity patterns, mobility, physical activity, vision impairment, older adults.

Manuscript word count: 3610

## **Abstract**

**Purpose:** To define and quantify patterns of objectively measured daily physical activity by level of visual field (VF) damage in glaucoma patients including: (1) activity fragmentation, a metric of health and physiological decline, and (2) diurnal patterns of activity, a measure of rest/activity rhythms.

**Design:** Prospective cohort study.

**Subjects:** Older adults diagnosed with glaucoma or suspected glaucoma.

**Methods:** Degree of VF damage was defined by the average VF sensitivity within the integrated VF (IVF). Each participant wore a hip accelerometer for one week to measure daily minute-by-minute activity for seven consecutive days. Activity fragmentation was calculated as the reciprocal of the average activity bout duration in minutes, with higher fragmentation indicating more transient, rather than sustained, activity. Multivariable linear regression was used to test for cross-sectional associations between VF damage and activity fragmentation. Multivariable linear mixed-effects models were used to assess the associations between VF damage and accumulation of activity across six time periods (5am-8am, 8am-11am, 11am-2pm, 2pm-5pm, 5pm-8pm, 8pm-11pm).

**Main Outcome Measures:** Activity fragmentation and amount of activity (steps) over the course of the day.

**Results:** Each 5-unit (dB) decrement in IVF sensitivity was associated with 16.3 fewer active minutes/day ( $p<0.05$ ), and 2% higher activity fragmentation ( $p<0.05$ ), but not with the number of active bouts/day ( $p=0.30$ ). In time-of-day analyses, lower IVF sensitivity was associated with fewer steps over the 11am-2pm, 2pm-5pm, and 5pm-8pm time periods (106.6, 93.1 and 89.2



fewer steps, respectively,  $p < 0.05$  for all), but not over other time periods. The activity midpoint (the time at which  $\frac{1}{2}$  of daily activity is completed) did not vary across level of VF damage.

Conclusions: At worse levels of VF damage, glaucoma patients demonstrate shorter, more fragmented bouts of physical activity throughout the day, and lower activity levels during typical waking hours, reflective of low physiological functioning. Further work is needed to establish the temporality of this association (i.e., whether these activity changes contribute to glaucoma disease severity, or are downstream effects), and whether glaucoma patients with such activity patterns are at a greater risk of the adverse health outcomes associated with activity fragmentation.

## Introduction

Physical activity is a central feature of well-being and an essential component of quality of life,<sup>1</sup> particularly in older adults, whose functional capability is often compromised,<sup>2</sup> physical activity declines,<sup>3</sup> and the risk of transitioning to assisted-living increases.<sup>4</sup> Previous research has established the importance of daily physical activity intensity and duration to health, yet emerging evidence suggests patterns of daily physical activity may provide insights into health and functional status with aging beyond these traditional measures.<sup>5-9</sup> Accelerometers are not only more precise and accurate than self-report of physical activity, they also allow minute-by-minute assessment of activity quantities and patterns throughout the day.<sup>10,11</sup> These patterns of physical activity have been associated with physical functioning, fatigability, disability, poor energy utilization/regulation, cognitive impairment, and overall mortality, independent of demographic, behavioral and medical history factors, and over and above traditional measures of physical activity.<sup>6,12-15</sup> Thus, understanding such complex patterns of activity in older adults who are largely affected by physical inactivity and sedentary behaviors, provides an indicator of future health and risk of functional decline.

Visual impairment from several conditions has been associated with lower physical activity,<sup>16-19</sup> with studies specifically demonstrating associations between VF damage and lower amounts of objectively measured daily activity, and less time spent in moderate and vigorous physical activity (MVPA).<sup>3,16,20</sup> Although previous research has found VF damage impacts time spent in MVPA to a similar degree as other systemic conditions (such as arthritis, diabetics, and stroke),<sup>3</sup> the impact of visual damage on patterns of daily physical activity is less studied. For example, daily physical activity becomes less frequent and intense, shorter in length, and more fragmented

with age,<sup>6</sup> marking individuals with low physical capacity and endurance,<sup>6,21</sup> and higher future mortality.<sup>22,23 5</sup> However, the associations between visual deficits with novel measures of activity patterns, such as the degree of fragmentation (i.e., more rapid switching from an active state to a sedentary state) or diurnal patterns of activity, remain uncharacterized.

Previous research focusing on diurnal activity patterns,<sup>24</sup> or how physical activity is accumulated throughout the day,<sup>15,25</sup> has also shown that older individuals reach their peak activity earlier in the day, and become less active as the day progresses.<sup>11</sup> However, no evidence has reported whether VF damage affects physical activity at specific hours of the day, which could yield insights into the underlying mechanisms between VF damage and low daily physical activity,<sup>26 4</sup> and highlight opportunities for future interventions.

This study compared two measures of daily activity patterns in glaucoma patients with VF damage: (1) activity fragmentation, and (2) diurnal patterns of activity. We used data from the Falls in Glaucoma Study (FIGS), an established population-based cohort of community-dwelling older adults with glaucoma.<sup>27</sup> We hypothesized that glaucoma patients with worse VF would exhibit more fragmented activity, and show lower activity in certain times (i.e., afternoon vs. morning), which could indicate a predisposition of some glaucoma patients to adverse health outcomes.

## **Methods**

This research adhered to the Declaration of Helsinki. The study was approved by the Johns Hopkins Institutional Review Board, and written consent was obtained from all participants.

### *Study Population*

The Falls in Glaucoma Study (FIGS) was a prospective and community-based cohort study conducted at Johns Hopkins Wilmer Eye Institute. The eligibility criteria of FIGS were described elsewhere.<sup>28,29</sup> In brief, participants were included if they were at least 60 years of age by study completion, lived within 60 miles from the hospital, could perform visual field (VF) testing, and were diagnosed with glaucoma or suspected glaucoma.<sup>28</sup> Patients were excluded if they had evidence of severe activity restriction (i.e., bed or wheelchair bound), had a visual acuity worse than 20/40 due to diseases other than glaucoma, or had undergone surgery (ocular or non-ocular) within the last two months.<sup>28</sup>

### *Vision Assessment*

Visual acuity was tested using ETDRS charts and converted to logMAR values. VF examination was performed using the Humphrey HFA-2 perimeter (Carl Zeiss Meditec, Carlsbad, California, USA). All VFs were screened for reliability by a glaucoma specialist (PR) based on reliability measures and consistency with prior testing results (i.e., excluding those with extraordinary changes inconsistent with a participant's clinical course).<sup>30</sup> Integrated VF (IVF) sensitivity was derived from right and left eye 24-2 VF tests by combining pointwise sensitivities for each VF location, and using the maximum sensitivity approach to generate the sensitivity at each spatial coordinate.<sup>28,31</sup> Next, each decibel sensitivity value in the IVF was converted to a raw (unlogged) sensitivity value, averaged across all points in the full VF, and then reconverted to a decibel (dB) value to derive mean sensitivity.<sup>28</sup> The mean IVF sensitivity for people with normal VFs falls in the range of 31 dB or above, with lower values indicating VF damage.<sup>27</sup> We

categorized the degree of VF damage as:<sup>32</sup> normal/mild (IVF >28 dB), moderate (IVF 23-28 dB), and severe (IVF <23 dB), with these categories roughly corresponding to the level of better-eye VF damage in normal/mild, moderate, and severe glaucoma as described by Hodapp, Parrish, and Anderson.<sup>32</sup>

### *Physical Activity Measurements*

FIGS participants wore a waist-bound accelerometer (Actical, Respironics Inc, Murrysville, PA) for seven days after their initial study visit during all waking hours except while swimming or bathing. Study coordinators called participants  $\geq 2$  times during their seven-day wear period to promote and maximize device adherence. For this analysis, data were used from participants who wore the device for a minimum of four valid days,  $\geq 8$  hours/day (97% of overall study participants).<sup>20,33</sup> Steps from the minute-by-minute level accelerometer data were used to calculate total daily physical activity and the amount of activity at different periods of the day. Minutes with any steps were classified as active minutes while minutes with no steps recorded were considered sedentary minutes.<sup>34</sup>

Similar to prior studies, active bouts were defined as consecutive minutes spent in an active state (i.e., any minute with one or more steps), and average bout duration was calculated as the total number of active minutes per day divided by the number of bouts per day.<sup>34</sup> Activity fragmentation (i.e., the Active-to-Sedentary Transition Probability)<sup>6,21</sup> was calculated as the probability of a transitioning from an active state to a sedentary state, which was equal to the reciprocal of the average bout duration (in minutes). Average activity fragmentation for a person was derived from averaging fragmentation per day across all valid days. Higher fragmentation

values reflect shorter, more fractured bouts of continuous activity (i.e., briefer episodes of activity).<sup>21</sup> For example, a fragmentation value of 0.4 (40%) indicates that, for that person/group, there is a 40% chance of an active minute being followed by a sedentary minute (as opposed to another active minute), while a value of 20% indicates a lower chance of an active minute being followed by a sedentary minute as a result of more sustained activity (longer activity bouts). For a given duration of physical activity (non-sedentary minutes), greater fragmentation would imply a larger number of bouts required to generate this physical activity, though greater fragmentation can also be seen with normal numbers of activity bouts in persons who spend less time in physical activity.

Average daily steps were derived by averaging total step counts across valid days. Additionally, for each participant, average steps taken during over 3-hour intervals spanning typical waking hours (5:00 am to 7:59 am, 8:00 am to 10:59 am, 11:00 am to 1:59 pm, 2:00 pm to 4:59 pm, 5:00 pm to 7:59 pm, and 8:00 pm to 10:59 pm) were calculated.<sup>11</sup>

### *Covariates*

Covariates including age, sex, race, living arrangement, and education were determined via questionnaires. We defined polypharmacy as taking  $\geq 5$  systemic prescription medications through the use of directly observed medications or a self-reported questionnaire.<sup>35</sup> We described the number of non-visual comorbidities from a previously-described list of comorbid conditions, including diabetes, stroke, arthritis, hip fracture, back problems, heart attack, angina, congestive heart failure, peripheral vascular disease, hypertension, emphysema, asthma, Parkinson's, non-skin cancer, and vertigo/Meniere's.<sup>33</sup> We evaluated cognitive function using the Mini-Mental

State Examination-Vision Impairment (MMSE-VI, maximum score=22), which classified dementia as a score  $\leq 16$  and no dementia as 17-22.<sup>36</sup>

### *Statistical Analysis*

Participant characteristics and activity metrics were described as means and proportions.

Differences in activity across the range of IVF sensitivity were evaluated using Pearson's  $\chi^2$  testing for categorical variables and *t*-test for continuous variables.

We fit a locally weighted scatterplot smoothing (LOWESS) plot to visualize activity fragmentation across the severity of glaucoma damage (Figure 1). Multivariable linear regression was used to test for associations between IVF sensitivity and active minutes and active bouts per day, and activity fragmentation, adjusting for the following covariates: age, sex, race, living arrangement, education, polypharmacy, number of comorbidities, and MMSE-VI.

To examine activity patterns over the day, mean unadjusted steps per hour were evaluated for persons with no/mild, moderate, and severe VF damage (Figure 2) and mean steps per hour for each 3-hour period of the day were plotted across the spectrum of IVF sensitivity (Supplementary Figure 1). Multivariable linear mixed effect models accounting for correlations between daily time periods and days of the week were used to examine how physical activity levels differed across six time intervals of the day varied by IVF sensitivity. Time-of-day intervals were treated as random effects and an unstructured covariance model was used to account for within-participant clustering. An interaction term between the fixed effect variables of time-of-day intervals and IVF sensitivity was added to evaluate whether average steps differed

across the time-of-day intervals by VF groups.<sup>15</sup> The contrast statements were used to compute the coefficients and 95% confidence intervals (CIs) to test average steps differences between VF damage groups at each time-of-day interval, respectively. To examine whether persons with worse VF damage shift their activity to an earlier or later time of the day, we used multivariable linear regression to assess whether IVF sensitivity was associated with activity initiation (the time at which 5% of daily activity is completed since first step after midnight), midpoint (the time at which 50% of daily activity is completed) and completion (the time at which 95% of daily activity is completed ). Statistical significance was determined using two-tailed hypothesis testing with an alpha of 0.05. All analyses were conducted using STATA 15.0 (StataCorp LP, College Station, Texas, USA).

## **Results**

For the 237 participants in the study population, the mean age was 70.6 (SD=7.6), 51.5% were men, and 70.9% had bachelor's degrees or higher. Roughly two-thirds (65%) of participants had at least two comorbidities, 4% had stroke and 46% had arthritis. 45.1% used five or more prescription medications, and the average MMSE-VI score was 20 (SD=1.6). Roughly half (48.9%) of participants had mild or normal IVF sensitivity, while 42% and 11% had IVF sensitivity reflecting moderate and severe VF damage, respectively (Table 1). Participants with moderate and severe VF damage were more likely to be African American, to live alone and have diabetes. With regards to activity measures, the number of active minutes varied across persons with normal/mild, moderate and severe VF damage (ANOVA  $p<0.01$ ), with the lowest number of active minutes noted in persons with severe VF damage. However, the number of active bouts per day remained similar across three VF damage groups (ANOVA  $p=0.10$ ).



Activity fragmentation was noted to vary across persons with severe, moderate and normal/mild VF damage (ANOVA  $p < 0.01$ ), with the highest fragmentation seen in those with severe VF damage (41%, SD=12%), and less fragmentation seen in those with moderate VF damage (33%, SD=9%) and normal VFs/mild VF damage (30%, SD=6%). Over the observed range of VF damage, greater fragmentation was observed with greater VF damage (Figure 1).

In continuous analyses, after adjusting for age, sex, race, living arrangement, education, polypharmacy, number of comorbidities, and MMSE-VI, each 5-unit (dB) decrement in IVF sensitivity was associated with 16.3 fewer active minutes per day (95% CI, -28.4 to -7.1). No associations were noted, however, between IVF sensitivity and the number of active bouts per day (mean=-7.7/5 dB decrement in IVF sensitivity, 95% CI, -15.7 to 0.3). More fragmented daily activity was present at greater levels of VF damage (2% higher/5 dB decrement in IVF sensitivity, 95% CI, 1% to 4%) (Table 2). In comparisons across level of VF damage, participants with more severe VF damage spent 67.6 fewer active minutes per day (95% CI, -103.4 to -31.8) compared to those with normal/mild VF damage, but had a similar number of active bouts per day (mean=-7.7/5 dB decrement in IVF sensitivity, 95% CI, -15.7 to 0.3). More fragmented activity was found in participants with severe VF damage (9% higher, 95% CI, 6% to 12%) compared to those with normal/mild VF damage; those with moderate VF group, however, did not show significant differences in any of the three activity outcomes (daily active minutes, daily activity bouts, and fragmentation). Other covariates associated with one or more activity outcomes included age, sex, education and comorbidity.

#### *VF damage and diurnal activity patterns*

For the full study population, average steps per hour began to increase between 7:00 am to 8:00 am, peaked between 12:00 pm to 2:00 pm, and declined between 5:00 pm to 6:00 pm (Figure 2). Participants with less VF damage took more steps between 11:00 am and 8:00 pm (Supplementary Figure 1). After adjusting for age, sex, race, living arrangement, education, polypharmacy, number of comorbidities, and MMSE-VI, each 5-unit (dB) decrement in IVF sensitivity was associated with 106.6 (95% CI, -197.1 to -16.1), 93.1 (95% CI, -182.1.0 to -4.2) and 89.2 (95% CI, -174.4.4 to 0) fewer steps between 11:00 am –2:00 pm, 2:00 pm – 5:00 pm, and 5:00 pm – 8:00 pm, respectively (Table 3). In categorical analyses of VF groups, participants with severe VF damage were significantly less active in each 3-hour time period between 11:00 am to 8:00 pm as compared to those with normal VFs/mild VF damage (Figure 2) exhibiting: 379.1 fewer steps per hour (95% CI, -649.6 to -108.5) from 11:00 am to 2:00 pm; 339.0 fewer steps per hour (95% CI, -604.9 to -73.2) from 2:00 pm to 5:00 pm; and 254.9 fewer steps per hour (-518.7 to -0.9) from 5:00 pm to 8:00 pm (Table 3). Participants with moderate VF damage group had similar amounts of activity over each 3-hour interval as compared to those with normal VFs/mild VF damage ( $p>0.05$  for all).

Over the 11:00 am to 8:00 pm period when most activity occurred, no interactions were noted between the degree of VF damage and time period with regards to activity participation, suggesting that persons with more advanced damage were uniformly less active throughout the day. Additional analyses of the time required to complete various portions of total daily activity, which reflect easier fatigability over the course of the day, did not show an association with VF damage, i.e., participants reached activity initiation (5% of daily activity), midpoint (50% of

daily activity) and completion (95% of daily activity) at similar times across the spectrum of VF severity (Table 4).

## **Discussion**

In the present study, we examined patterns of daily activity in persons with a range of VF damage from glaucoma using two novel measures of physical activity: activity fragmentation (i.e., the probability of an active state to an inactive state), and diurnal patterns of daily activity. At worse levels of VF damage, physical activity was lower and more fragmented during typical waking hours, despite having a similar number of active bouts, demonstrating less sustained activity throughout the day. However, the activity midpoint (the time at which  $\frac{1}{2}$  of daily activity is completed) did not vary across level of VF damage, suggesting that although those with more advanced damage were less active overall, they did not frontload or backload their daily activity. Collectively, these results demonstrate that glaucoma patients have a tendency to perform less daily activity and transition out of an active state to a sedentary state more quickly.

Our findings support prior research that found VF damage to be associated with lower physical activity in glaucoma patients,<sup>16,20</sup> and extend these findings by demonstrating that restriction of activity participation occurs roughly equally across the period of the day when activity typically takes place (i.e. 11 am – 8 pm). While some prior studies used subjective activity assessments (e.g., recall surveys and activity diaries),<sup>37-39</sup> data from these instruments are often subject to recall bias and activity misclassification.<sup>40</sup> More recent work has demonstrated that VF damage is associated with lower overall objectively-defined physical activity,<sup>3</sup> but activity patterns across the full spectrum of the day were not explored.

While previous research mainly focused on total volume of activity (e.g., steps or counts) or time spent in more intense activity (e.g., MVPA),<sup>3,41,42</sup> our study examined patterns of activity accumulation throughout the day. Importantly, we found that worse VF damage was associated with more fragmented daily activity (i.e., active bouts were shorter), resulting in lower accumulation of activity. While previous research has not looked at the relationship between vision and activity fragmentation, others have noted that more fragmented activity is associated with older age, slower gait, higher fatigability, lower functioning and higher risk of mortality.<sup>5,6,21</sup> These results suggest that activity fragmentation is an important measure of health independent of total activity performed, and suggest that specific glaucoma patients, i.e. those with more fragmented activity associated with worse VF damage, might be at higher risk of adverse outcomes that have been associated with activity fragmentation, i.e., poor physical functioning<sup>6</sup> and death.<sup>5</sup>

Previous studies have suggested that altered or lower diurnal activity patterns are indicative of a greater risk of falls and higher fatigability.<sup>7,15,43</sup> Our evaluation of differences in diurnal patterns of activity by VF damage were found to be in line with prior studies using wearable devices, with participants beginning their activities around 7:00 am, reaching maximum activity around noon, and decreasing activity late in the afternoon or evening.<sup>11,15</sup> Of note, persons with greater VF damage were not observed to restrict their activity more during the later period of the day; in other words, activity was not shifted to the hours closer to waking time at worse levels of VF damage. Of note, if late-day declines in activity occur as a result of fatigue later in the day, such declines may not be present in those with greater VF damage given their low levels of activity.

Likewise, greater declines in activity may have been expected later in the day because of greater difficulty with activity in poor lighting in glaucoma patients;<sup>44</sup> though it is possible that such difficulties can be overcome with proper home lighting, or that they are just difficult to observe in our data due to the low level of late day activity even in persons with minimal or normal VF damage.

The meaning of our findings would ideally shed light on the temporal relationship between glaucoma damage and physical activity. However, the relationship between glaucoma damage and activity in humans remains unclear. While mouse studies have suggested that exercise can prevent IOP-induced damage to the optic nerve,<sup>45</sup> human studies relating physical activity to glaucoma damage are cross-sectional or inconclusive regarding whether VF damage precedes lower physical activity or vice versa.<sup>20</sup> If physical activity is indeed protective against glaucoma damage in humans, and our study participants with worse VF experience this damage partially as a result of their declining activity levels, then our results raise the question of whether the pattern of activity is also relevant to the onset and worsening of glaucoma. In this model, less fragmented activity (i.e. longer bouts of activity) would be important in protecting against glaucoma – ideas that need to be further explored in longitudinal studies and/or clinical trials. If low physical activity is a downstream consequence of visual field damage from glaucoma, then our results suggest that this visual damage may lead individuals to engage in shorter bouts of activity, contributing to lower activity levels overall. Identifying the factors leading to greater VF damage, including higher fatigability or intraocular pressure, may help increase activity levels, which in turn could improve overall health. Finally, common factors, i.e. poor fitness or energetics, may lead to both glaucomatous VF damage and further declines in physical activity.

In this model, improving this latent factor would hold potential both for reducing glaucoma damage and improving physical activity, which may enhance overall well-being.

Our study has limitations. First, our study has limited generalizability as study participants were enrolled from a single center with a single visual condition - glaucoma. Second, the cross-sectional design limits the ability to assess whether higher activity fragmentation follows or proceeds VF damage in glaucoma, which warrants further testing in longitudinal analyses. Third, we did not obtain more details of comorbidities that could impact physical activity, that is, the severity and duration of each comorbid condition, and any interactions between these comorbidities. Fourth, although fragmentation captures the reduced and altered activity patterns, it may not provide insights into other patterns of activity which represent all aspects of declining health, e.g., aerobic activity and metabolic capacity.<sup>46</sup> Fifth, the accelerometer does not capture upper body movement and other types of activities, e.g., swimming and bicycling.

In summary, our study found that glaucoma patients with worse levels of VF damage complete their activity in shorter bouts and demonstrate lower activity levels during typical waking hours. However, their activity does not appear to diminish over the course of the day. Further work is needed to establish the temporality of the cross-sectional findings, i.e., whether these activity changes contribute to glaucoma disease severity, or are downstream effects. Additional future studies are necessary to assess whether these results could apply to other ocular disorders (e.g., cataract, diabetic retinopathy). Given the associations between more fragmented activity and physiological decline, our findings suggest possible physical health consequences to in some glaucoma patients, i.e. those with more fragmented activity due to severe VF damage.

## **Acknowledgement**

The research was supported in part by National Institutes of Health Grant EY022976.

## **Conflict of Interest**

Authors have no conflict of interest to declare.

## **CRedit authorship contribution statement**

**Jian-Yu E:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Validation, Visualization, Writing - original draft, Writing - review & editing.

**Jennifer A. Schrack:** Conceptualization, Methodology, Supervision, Writing - review & editing. **Aleksandra Mihailovic:** Data curation, Project administration, Validation, Writing - review & editing. **Amal A. Wanigatunga:** Conceptualization, Methodology, Writing - review & editing. **Sheila K. West:** Funding acquisition, Methodology, Validation, Writing - review & editing. **David S. Friedman:** Funding acquisition, Methodology, Validation, Writing - review & editing. **Laura N. Gitlin:** Funding acquisition, Methodology, Validation, Writing - review & editing. **Tianjing Li:** Conceptualization, Methodology, Supervision, Writing - review & editing. **Pradeep Y. Ramulu:** Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing - review & editing.

## **Sponsor's Role:**

The founding organization play no role in the design and conduct of this research.

Table 1. Participant characteristics and activity metrics by severity of glaucoma damage (N=237)

	Normal/Mild VF damage (IVF: >28 dB) N = 116	Moderate VF damage (IVF: 23-28 dB) N = 96	Severe VF damage (IVF: <23 dB) N = 25	P-value
<b>Demographic and clinical characteristics</b>				
Age, mean (SD)	69.15 (6.45)	72.33 (8.75)	70.40 (7.09)	0.04
Male, n (%)	58 (50)	52 (54)	12 (48)	0.78
African American, n (%)	28 (24)	24 (25)	17 (68)	<0.01
Living alone, n (%)	19 (16)	22 (23)	7 (28)	0.03
Education				0.14
≤ High school, n (%)	15 (13)	16 (18)	6 (24)	
Some college, n (%)	14 (12)	13 (14)	5 (20)	
Bachelor, n(%)	34 (29)	19 (20)	6 (24)	
≥ Master, n (%)	53 (46)	48 (50)	8 (32)	
Polypharmacy, n (%)	47 (41)	44 (46)	16 (64)	0.10
No. of comorbidities				0.88
≤ 1, n (%)	38 (33)	36 (38)	9 (36)	
2-3, n (%)	52 (45)	42 (43)	11 (44)	
4-5, n (%)	26 (22)	18 (19)	5 (20)	
Diabetes (%)	21 (18)	27 (28)	10 (40)	0.04
Stroke (%)	3 (3)	5 (5)	1 (4)	0.60
Arthritis (%)	55 (47)	45 (47)	10 (40)	0.79
MMSE-VI, mean (SD)	20.32 (1.50)	19.66 (2.18)	19.84 (1.84)	0.03
<b>Activity variables</b>				
Active minutes per day	252.04 (76.64)	237.08 (88.24)	176.02 (83.21)	<0.01
No. of bouts per day	70.07 (15.32)	69.68 (18.10)	63.00 (24.25)	0.10
Fragmentation	0.30 (0.06)	0.33 (0.09)	0.41 (0.12)	<0.01

VF: vision field; SD: standard deviation; Polypharmacy: ≥ 5 systemic prescription medications; MMSE-VI: Mini-Mental State Examination-Vision Impairment (maximum as 22); dB: decibels; Fragmentation: probability of an active state to an inactive state; IVF: integrated vision field.



Table 2. Associations between severity of glaucoma damage and activity outcomes in multivariable models (N=237)

Variables	Active minutes per day $\beta$ (95% CI)	No. of bouts per day $\beta$ (95% CI)	Fragmentation $\beta$ (95% CI)
5-unit (dB) decrement in IVF sensitivity <sup>a</sup>	-16.26 (-28.43, -4.09)**	-1.15 (-3.85, 1.55)	0.02 (0.01, 0.04)**
VF damage <sup>a</sup>			
Normal/Mild	Reference	Reference	Reference
Moderate	-4.72 (-26.55, 17.10)	0.43 (-4.45, 5.31)	0.01 (-0.01, 0.03)
Severe	-67.60 (-103.43, -31.78)**	-7.71 (-15.73, 0.30)	0.09 (0.06, 0.12)**

<sup>a</sup>Severity of VF damage on continuous and categorical scale were derived from different models, each containing the same covariates: age, race, sex, living arrangement, education, comorbidity, polypharmacy, and cognitive function.

Fragmentation: probability of an active state to an inactive state; VF: vision field; IVF: integrated vision field; dB: decibels; CI: confidence interval; Polypharmacy:  $\geq 5$  systemic prescription medications; Mini-Mental State Examination-Vision Impairment (maximum as 22).

\*p <0.05, \*\*p <0.01

Table 3. Interaction between time-of-day intervals (5:00 am to 11:00 pm) and severity of glaucoma damage on daily steps (N=237)

Time	5-unit (dB) decrement in IVF ( $\beta$ , 95% CI)	VF damage ( $\beta$ , 95% CI)		
		Normal/Mild	Moderate	Severe
5:00 am–8:00 am	-6.38 (-102.34, 89.78)	Reference	-46.81 (-224.96, 131.33)	-23.84 (-311.17, 263.49)
8:00 am–11:00 am	-49.83 (-142.67, 43.02)	Reference	-9.55 (-181.66, 162.56)	-244.29 (-522.07, 33.49)
11:00 am–2:00 pm	-106.61 (-197.09, -16.12)*	Reference	59.97 (-107.57, 227.52)	-379.08 (-649.64, -108.52)**
2:00 pm–5:00 pm	-93.12 (-182.05, -4.19)*	Reference	-4.33 (-168.90, 160.24)	-339.04 (-604.89, -73.19)*
5:00 pm–8:00 pm	-89.19 (-174.41, -0.04)*	Reference	-57.93 (-221.20, 105.35)	-254.92 (-518.72, -0.89)*
8:00 pm–11:00 pm	-14.73 (-102.12, 73.66)	Reference	-5.51 (-169.20, 158.13)	-76.25 (-340.71, 188.21)

Mixed effects estimates adjusted for age, race, sex, living arrangement, education, comorbidity, polypharmacy, and cognitive function.

VF: vision field; IVF: integrated vision field; dB: decibels; CI: confidence interval.

\* $p < 0.05$ , \*\* $p < 0.01$

Table 4. Severity of glaucoma damage on time to accumulate total daily activity (N=237)

Time (hour)	5-unit (dB) decrement in IVF ( $\beta$ , 95% CI)	Vision field damage ( $\beta$ , 95% CI)		
		Normal/Mild	Moderate	Severe
Time to reach 5% of daily activity	-0.13 (-0.45, 0.19)	Reference	0.16 (-0.80, 1.12)	0.04 (-0.92, 0.99)
Time to reach 50% of daily activity	0.02 (-0.37, 0.42)	Reference	0.03 (-1.15, 1.21)	-0.14 (-1.31, 1.04)
Time to reach 95% of daily activity	0.06 (-0.33, 0.44)	Reference	0.03 (-1.12, 1.18)	-0.22 (-1.36, 0.92)

Adjusted for age, race, sex, living arrangement, education, comorbidity, polypharmacy, and cognitive function. IVF: integrated vision field; dB: decibels; CI: confidence interval.

Figure 1. Locally weighted scatterplot smoothing (LOWESS) plot of activity fragmentation by severity of glaucoma damage.

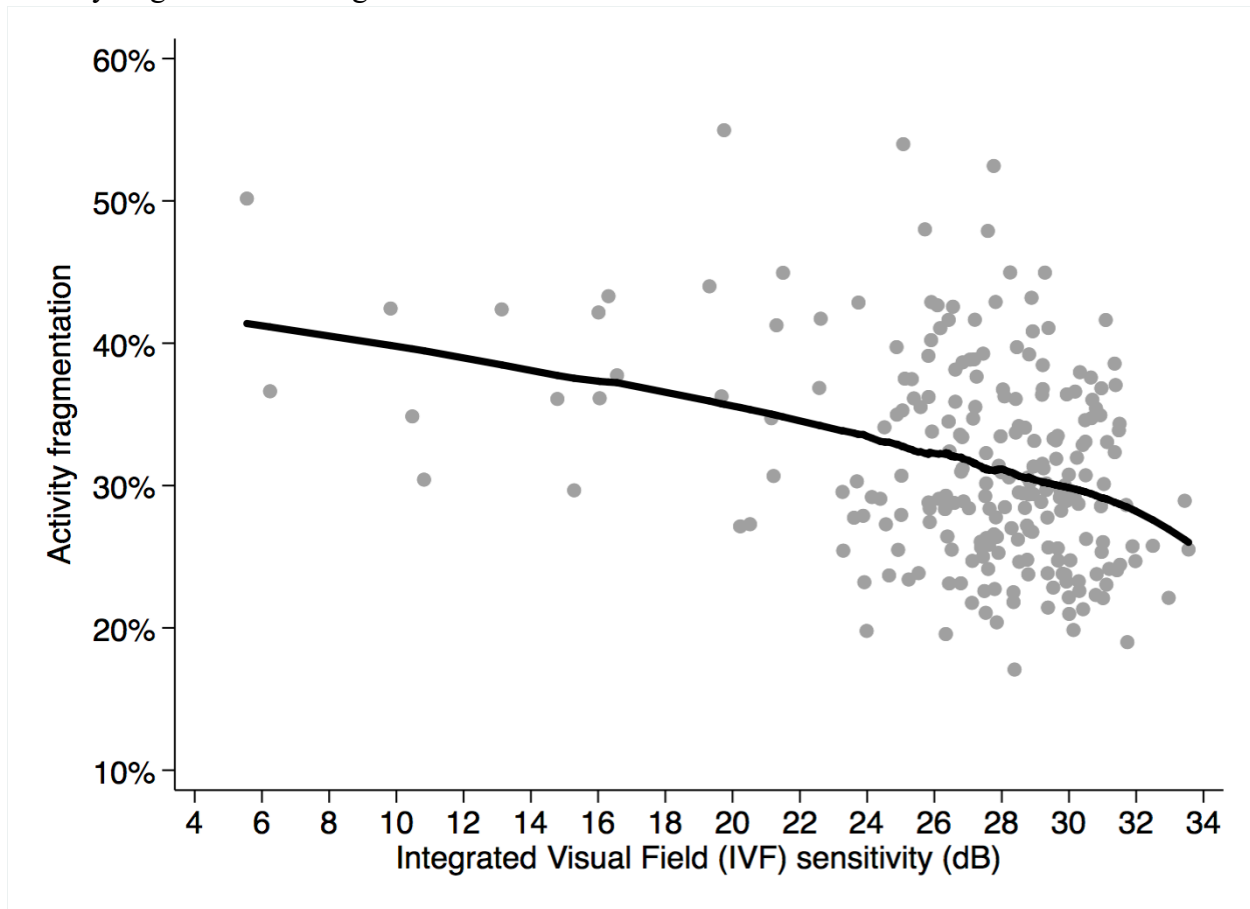
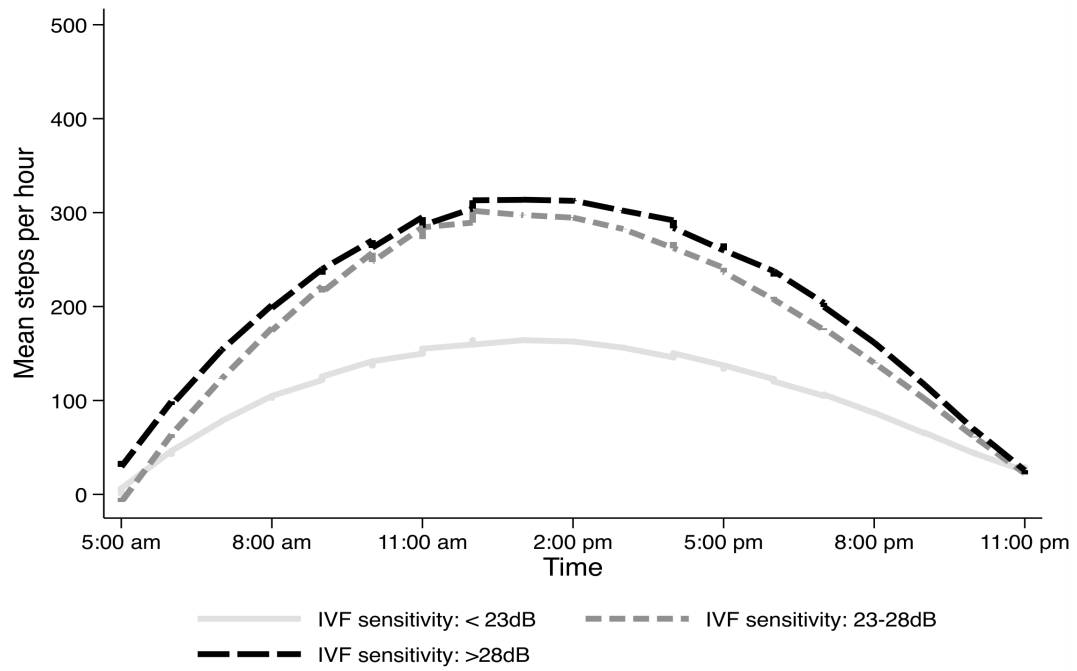
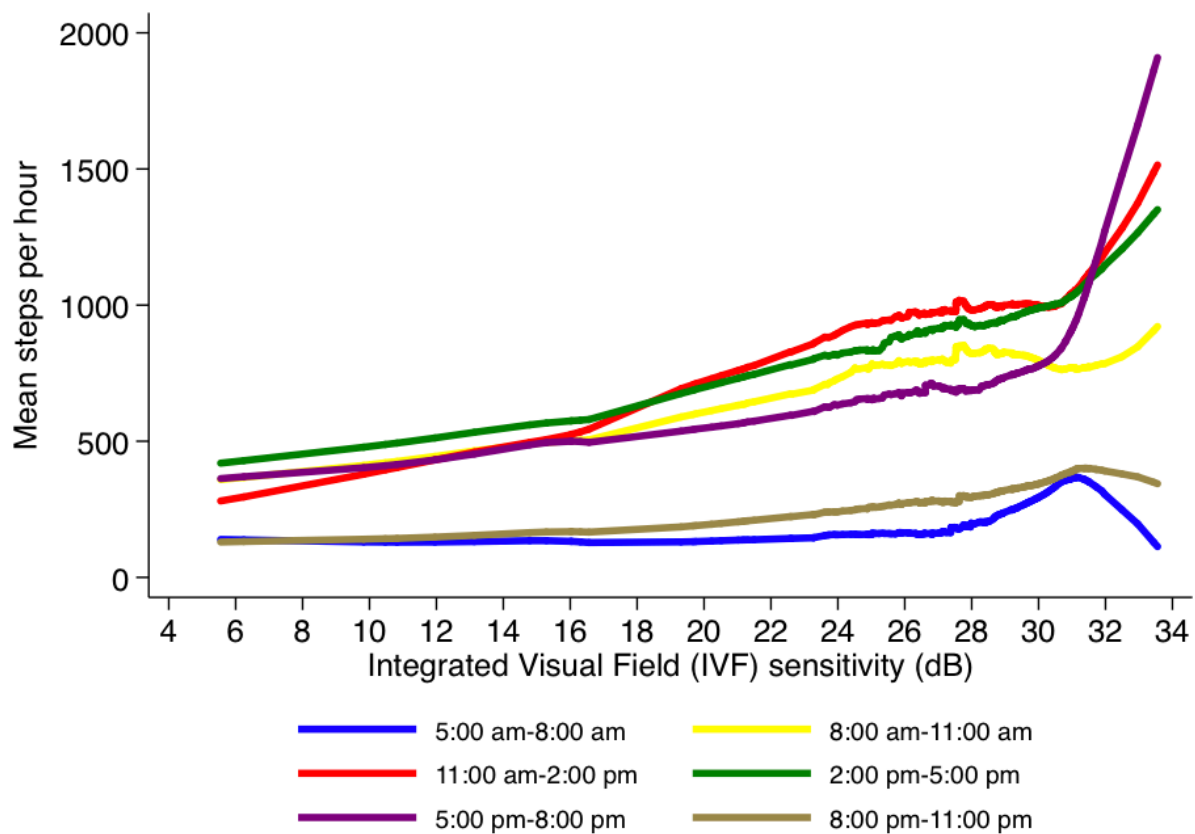


Figure 2. Mean steps per hour during 5:00 am to 11:00 pm stratified by severity of glaucoma damage.



Supplementary Figure 1. Mean steps per hour by severity of glaucoma damage at every 3-hour interval from 5:00 am to 11:00 pm.



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## Chapter 5

### Conclusion

Fall prevention in visually impaired older adults is highly relevant to patients, caregivers, providers, insurers, and policy makers as the older population grows dramatically. However, assessing the effectiveness of fall prevention strategies without addressing activity restriction has major limitations because those with fear of falling (FoF) can reduce daily physical activity to avoid falling. The research presented in this dissertation uncovers the impact of FoF on activity restriction and future falls as essential components of quality of life, and characterizes the novel measures of activity patterns to provide insights into health and functional status. Collectively, the results from this dissertation provide critical information towards developing an intervention protocol and clinical trial to reduce falls and improve physical activity in visually impaired population.

Manuscript 1 systematically reviewed the literature about the current strategies to prevent falls and reduce physical activity limitations among visually impaired older adults. There was no evidence of an effect for most of the environmental or behavioral interventions studied for preventing falls and reducing physical activity limitation in visually impaired older people. The certainty of the evidence is generally low due to poor methodological quality and heterogeneous outcome measurements. Moreover, results from Manuscripts 2 and 3 suggest that future fall prevention trials should plan to use objectively measured or self-reported physical activity as outcome measures, to reduce confounding by activity limitation. This implies that fall

preventions strategies should evaluate the acceptability and applicability of interventions, and assess the adherence to rehabilitative strategy and performance during activities of daily living.

Manuscript 2 explored the within-subject changes in fall rates and physical activity associated with changes in FoF in older adults with varying degrees of visual impairment. We found that the implications of FoF on mobility (falls and physical activity) depended on the level of FoF. At lower FoF levels, increases in FoF were associated with a higher risk of falls, but not activity decline; however, at higher levels of FoF, increases in FoF did not increase the risk of falls, but were associated with declines in physical activity. These results suggest that physical activity declines may result only after FoF reaches a certain threshold, and that the consequences of FoF are not uniform. These findings highlight the necessity of future studies to examine whether interventions that target FoF will have an impact on future falls or activity changes.

Manuscript 3 investigated the patterns of daily activity in persons with a range of visual damage from glaucoma using two novel measures of physical activity: activity fragmentation and diurnal patterns of daily activity. We found that glaucoma patients with worse levels of visual field damage complete their activity in shorter bouts and demonstrate lower activity levels during typical waking hours. However, their activity does not appear to diminish over the course of the day. Collectively, these results demonstrate that glaucoma patients have a tendency to perform less daily activity and transition out of an active state to a sedentary state more quickly. Given the associations between more fragmented activity and physiological decline, our findings suggest possible physical health consequences in some glaucoma patients, and highlight opportunities for future interventions.

Together, the three papers presented in this dissertation: (1) systematically review the current strategies to prevent falls and reduce physical activity limitations, (2) provide evidence that supports the hypothesis that FoF serves as an indicator for future falls and physical activity, and (3) delineate activity fragmentation and diurnal patterns of activity in persons with various severity of vision damage. These results shed light on directions for future research in visually impaired older adults, including: (1) a consensus to adopt core outcomes for falls and physical activity research, (2) investigating early predictors of falls and functional decline, and (3) designing clinical trials to reduce falls and improve mobility.

Overall, this dissertation identifies, selects, appraises and summarizes relevant literature about interventions to prevent falls and improve physical activity in visually impaired older adults that are vital to promoting public health. Falls in Glaucoma Study (FIGS), a well-characterized and population-based cohort, allows us to assess falls prospectively which minimizes recall bias and capture minute-by-minute physical activity amongst visually impaired older adults longitudinally, which to the best of our knowledge, has never been done before. Moreover, characterizing distinctive activity patterns among visually impaired older adults provide an opportunity for recognizing indicators of future health and risk of functional decline, and hence addressing modifiable risk factors in fall prevention. Our research has limitations. These findings may not be generalizable to all older adults with vision loss because participants in FIGS were recruited from a single center with one condition (i.e., glaucoma). Additionally, it remains challenging to measure various types of physical activity patterns which represent all aspects of

declining health using the accelerometer. We therefore recognize the need for caution in the interpretation of our results.

In summary, this research contributes to our understanding of the role of two modifiable lifestyle factors, falls and physical activity, in the maintenance of overall well-being in visually impaired older adults. These studies serve as the first step to promote the physical activity status and impact treatment directions for this growing yet undertreated population. More work is warranted to identify causal modifiers of fall reduction that may be safely intervened upon to prevent or postpone physical activity decline in older adults with visual impairment.

*Healthy People 2020* (<https://www.healthypeople.gov/2020>) has announced the perspectives towards health-related needs of people with visual disabilities. Given the ubiquitous influence of mobility decline in older adults with visual impairment, public health officials have set the objective to design and implement interventions to eliminate health disparities between people with and without vision loss. Three papers in this dissertation provide a foundation for developing evidence-based interventions to improve physical function and quality of life in visually impaired population by maximizing the use of remaining vision and by devising mobility aids to assist those without useful vision. Educating the families and communities about healthy and safe lifestyles is critical to ensuring that visually impaired older adults have the information, resources and tools needed for living with low vision.



# Curriculum Vitae

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## Education

<b>Johns Hopkins Bloomberg School of Public Health</b> <i>Doctor of Science (ScD) in Epidemiology</i> <i>Clinical Trials &amp; Evidence Synthesis</i>	<b>08/2017 – 08/2020</b>
<b>Rutgers University</b> <i>Master of Public Health (MPH) in Epidemiology</i>	<b>01/2015 – 12/2016</b>
<b>Dalian Medical University</b> <i>Bachelor of Medicine</i>	<b>10/2007 – 07/2012</b>

## Summary of Skills

### Systematic and targeted literature review

- Performed systematic reviews to support health technology assessment.
- Conducted meta-analysis and performed methodological research using a variety of approaches (single-arm trials and network meta-analysis), supported Institute of Clinical and Economic Research reviews.
- Developed search strategies for MEDLINE (Ovid), Embase, Cochrane Controlled Register of Trials (CENTRAL), Northern Light Life Sciences Conference Abstracts.

### Randomized controlled trials

- Designed and conducted randomized clinical trials, developed and evaluated methods for comparing healthcare interventions, drafted manuscripts and prepared publications for top-tier scientific journals.

### Real-world evidence

- Designed and performed studies using real-world data, including healthcare claims, electronic health records, designed surveys to assess patient reported outcomes (PROs).
- Assessed the burden of diseases, treatment patterns, adherence, medical resource utilization and costs, adverse events monitoring, and effects of treatment modification.

### Competencies

- Proficient skills in analytical software (STATA, SAS and R), machine learning algorithms, causal inference, survival analysis, longitudinal models, multi-level models, simulation models, structure equation models, decision analytic models, probabilistic sensitivity analysis, Markov modeling, cost-effective

analysis, cost-benefit analysis, microsimulation, agent-based models, Mplus, Qualtrics, Covidence, MS Office (Excel, PowerPoint, Word).

- Languages: English and Mandarin Chinese (native).

## **Professional Experience**

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### **Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health 10/2017 – 08/2020**

#### *Research Methodologist*

- Drafted manuscripts and prepared publications for top-rated scientific journals on subjects including literature reviews, randomized controlled trials, and comparative effectiveness research.
- Project management on all facets of research process including design, coordination and logistics, and conduct of research for Cochrane Eyes and Vision (CEV) US Projects, Center for Clinical Trials & Evidence Synthesis (CCTES), Center for Aging & Health (COAH), and Wilmer Eye Institute.
- Performed data collection, management, and analyses on a variety of topics pertaining to health care policy, utilization, implementation, safety and effectiveness.
- Managed project and CCTES journal clubs, workshops and seminars with leaders in academia, government, and healthcare industry.

### **Department of Population Science, Cancer Institute of New Jersey, Rutgers University 08/2015 – 07/2017**

#### *Statistician*

- Evaluated treatment patterns, outcomes, and costs among Medicare beneficiaries diagnosed with pancreatic cancer and prostate cancer using SEER-Medicare data; conducted statistical analyses and programming using SAS and SQL.
- Developed statistical analysis plans and research designs for oncology outcomes studies.
- Prepared manuscripts and abstracts for journal and conference submission.
- Wrote grants and developed operating budgets for federal funding opportunities.
- Managed projects through different stages, including data acquisition, IRB submissions.

### **Dallas Neuroscience Physician Association, Desoto, Texas 01/2013 –12/2014**

#### *Research Coordinator*

- Improved patient experience with care they received at Dallas Neuroscience.
- Worked with a team to develop and implement surveys that could assess patient satisfaction.
- Developed quality improvement protocol for clinic procedures performed by neurologists.
- Conceptualized and developed all aspects of the research projects: data collection, education intervention for technicians and data analysis plans.

- Designed and implemented a longitudinal study for patients with neurological disorders, managed the study by assuring smooth daily operations.
- Conducted research that required independence in designing experiments, troubleshooting and interpreting results.

**Department of Biology Science, Baylor University**  
**08/2012 – 12/2012**

*Visiting Student*

- Took professional courses, including “Statistical Methods”, “Cell Polarity”, “Research Methods in Biology” and “Special Problems”.

**Publications**

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1. **E JY**, Schrack JA, Wanigatunga A, Mihailovic A, West SK, Friedman DS, Gitlin LN, Li T, Ramulu PY. Patterns of daily physical activity across the spectrum of visual field damage in glaucoma patients. *Ophthalmology*. 2020. doi: 10.1016/j.opthta.2020.06.053.
2. **E JY**, Ramulu PY, Fapohunda K, Li T, Scherer RW. Frequency of abstracts presented at vision conferences being developed into full length publications: a systematic review and meta-analysis. *JAMA Ophthalmol*. 2020;138(6):1–10. doi: 10.1001/jamaophthalmol.2020.1264.
3. **E JY**, Mihailovic A, West SK, Friedman DS, Gitlin LN, Li T, Schrack JA, Ramulu PY. Characterizing the impact of fear of falling on accelerometer-defined physical activity and future falls in older adults with glaucoma. *J Am Geriatr Soc*. 2020. doi: 10.1111/jgs.16516. Epub ahead of print.
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5. **E JY**, Saldanha IJ, Canner J, Schmid CH, Le JT, Li T. Adjudication rather than experience of data abstraction matters more in reducing errors in abstracting data in systematic reviews. *Res Synth Methods*. 2020;11(3):354-362. doi: 10.1002/jrsm.1396.
6. **E JY**, Mihailovic A, Schrack JA, Li T, Friedman DS, West SK, Gitlin LN, Ramulu PY. Characterizing longitudinal change of physical activity and fear of falling in glaucoma patients. *Int J Epidemiol* (Under Review). 2020.
7. **E JY**,\* Wang Z,\* Ssekasanvu J, Munoz B, West SK, Ludigo J, Gray R, Nakigozi G, Kong X. Visual impairment and eye diseases in HIV-infected people in the antiretroviral therapy (ART) era in Rakai, Uganda. *Ophthalm Epidemiol*. 2020. doi: 10.1080/09286586.2020.1791908.

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12. **E JY**, Lu SE, Lin Y, Graber JM, Rotter D, Zhang L, Petersen GM, Demissie K, Lu-Yao G, Tan XL. Differential and joint effects of metformin and statins on overall survival of elderly patients with pancreatic adenocarcinoma: a large population-based study. *Cancer Epidemiol Biomarkers Prev*. 2017;26(8):1225-1232. doi: 10.1158/1055-9965.EPI-17-0227.
13. **E JY**, Graber JM, Lu SE, Lin Y, Lu-Yao G, Tan XL. Effect of metformin and statin use on survival in pancreatic cancer patients: a systematic literature review and meta-analysis. *Curr Med Chem*. 2018;25(22):2595-2607. doi: 10.2174/0929867324666170412145232.
14. Duan J, Yue W, **E JY**, Malhotra J, Yang CS, Lu SE, Gu J, Xu F, Tan XL. Comparative in vitro study of the effects of triacetylresveratrol on cell proliferation, apoptosis, and STAT3 and NFκB signaling in pancreatic cancer cells. *Sci Rep*. 2016;6(8):31672. doi: 10.1038/srep31672.
15. Liu Z, Wang A, Pu Y, Li Z, **E JY**, Xue R, Zhang C, Xiang X, Bu Z, Bai F, Ji J. Genomic and transcriptomic profiling of hepatoid adenocarcinoma of the stomach. *Gastroenterology* (Under Review). 2020

### Oral Presentations

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1. **E JY**, Schrack JA, Wanigatunga A, Mihailovic A, West SK, Friedman DS, Gitlin LN, Li T, Ramulu PY. Patterns of daily physical activity across the spectrum of visual field damage in glaucoma patients. The Association for Research in Vision and Ophthalmology (ARVO). 05/2020, Baltimore, MD. (<https://learning.arvo.org/diweb/catalog/item?id=5193436>)

2. **E JY**, Mihailovic A, West SK, Friedman DS, Gitlin LN, Li T, Schrack JA, Ramulu PY. Characterizing the impact of fear of falling on accelerometer-defined physical activity and future falls in older adults with glaucoma. The Association for Research in Vision and Ophthalmology (ARVO). 05/2020, Baltimore, MD
3. **E JY**, Saldanha IJ, Canner J, Schmid CH, Le JT, Li T. Does level of experience matter when abstracting data for systematic reviews. Cochrane Colloquium. 10/2019, Santiago, Chile. ([https://www.youtube.com/watch?v=dYTtHhiL\\_S4](https://www.youtube.com/watch?v=dYTtHhiL_S4))
4. **E JY**, Lu SE, Lin Y, Graber JM, Rotter D, Zhang L, Petersen GM, Demissie K, Lu-Yao G, Tan XL. Differential and joint effects of metformin and statins on overall survival of elderly patients with pancreatic adenocarcinoma: a large population-based study. Annual Retreat on Cancer Institute of New Jersey. 05/2017, New Brunswick, NJ
5. **E JY**, Graber JM, Lu SE, Lin Y, Lu-Yao G, Tan XL. Effect of metformin and statin use on survival in pancreatic cancer patients: a systematic literature review and meta-analysis. 4th NYC Epidemiology Forum (NYCEF) conference. 02/2017, Manhattan, NY.

#### Poster Presentations

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1. **E JY**, Ramulu PY, Fapohunda K, Li T, Scherer RW. Frequency of abstracts presented at vision conferences being developed into full length publications: a systematic review and meta-analysis International Society for Pharmacoeconomics and Outcomes Research (ISPOR). 05/2020, Orlando, FL.
2. Lu-Yao G, **E JY**, Lin Y, Rebbeck T, Lu SE, Kelly WK, D'Amico AV, Stein MN, Zhang L, Kim IY, Demissie K, Ferrari AC, Tan XL. Individual and joint effect of postdiagnostic metformin and statin use on prostate cancer mortality among patients with high-risk prostate cancer. American Association for Cancer Research. 04/2017. Washington D.C.
3. **E JY**, Lin Y, Rebbeck TR, Lu SE, Shang M, Kelly WK, D'Amico A, Stein MN, Zhang L, Jang TL, Kim IY, Demissie K, Ferrari A, Tan XL. Concomitant Metformin and Statin Use and Mortality in Patients with High-risk Prostate Cancer: A Population-based Study. Annual Retreat on Cancer Institute of New Jersey. 05/2017, New Brunswick, NJ.
4. Duan J, Yue W, **E JY**, Malhotra J, Yang CS, Lu SE, Gu J, Xu F, Tan XL. Comparative in vitro study of the effects of Triacetylresveratrol on cell proliferation, apoptosis, and STAT3 and NFκB signaling in pancreatic cancer cells. Annual Retreat on Cancer Institute of New Jersey. 05/2016, New Brunswick, NJ.

#### Editorial Board

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1. *American Journal of Clinical Oncology*  
(<https://journals.lww.com/amjclinicaloncology/Pages/editorialboard.aspx>)
2. *International Journal of Clinical Trials*  
(<https://www.ijclinicaltrials.com/index.php/ijct/about/editorialTeam>)

## Peer Reviewer

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1. *European Heart Journal*
2. *JAMA Network Open*
3. *International Journal of Behavioral Nutrition and Physical Activity*
4. *Clinical Trials*
5. *Trials*
6. *Systematic Reviews*
7. *American Journal of Ophthalmology*
8. *PLoS One*
9. *Journal of Glaucoma*
10. *Joanna Briggs Institute (JBI) Evidence Synthesis*
11. *Scientific Reports*

## Teaching Experience

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### **Johns Hopkins Bloomberg School of Public Health**

1. “340.648. Clinical Trials Management”
2. “340.861. Clinical Trials: Procedures, Design, and Interpretation of Results”
3. “340.645. Introduction to Clinical Trials”
4. “309.750. Applied Research Methods for Health Policy and Management”
5. “140.620. Advanced Data Analysis Workshop.”
6. “340.752. Epidemiologic Methods 2”
7. “340.751. Epidemiologic Methods 1”

### **Rutgers University School of Public Health**

8. “Applied Regression Analysis for Public Health Studies”

## News, Honors and Awards

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- American Association of Schools and Programs of Public Health – Friday Letter Report, 2020
- Johns Hopkins Bloomberg School of Public Health Student – EpiIDEAS Spotlight

- Campaign, 2020
- Healio News – “Declining Patterns of Physical Activity Related to Visual Field Damage”, 2020
  - Healio News – “Severity of Visual Field Damage Related to Daily Physical Activity”, 2020
  - HCPLive News – “Most Data from Major Ophthalmology Conferences Goes Unpublished”, 2020
  - Johns Hopkins Bloomberg School of Public Health Student Travel Support Fund, 2019
  - Excellent Student Scholarship, Chinese Medical Association, 2011

### **Social Activities**

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- Funding Chair, Epidemiology Student Organization, Johns Hopkins School of Public Health, 2018
- Journal Club Coordinator, Johns Hopkins School of Public Health, 2017